Right ventricular myocardial diastolic dysfunction in different kinds of cardiac hypertrophy: analysis by pulsed Doppler tissue imaging

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Right ventricle.

Background. **Right ventricular (RV) chamber involvement has been demonstrated in hypertrophic cardiomyopathy (HCM) as well as in hypertensive left ventricular hypertrophy (LVH) but little is known about RV myocardial dysfunction occurring in these two pathologies. The aim of this study was to compare Doppler tissue imaging (DTI) of the right ventricle in HCM and LVH in relation to DTI of the left ventricle and Doppler standard of the RV and left ventricular (LV) inflow.**

Methods. **Thirty controls, 20 hypertensives with LVH, and 23 patients with HCM involving the interventricular septum underwent Doppler echocardiography and pulsed DTI of the LV lateral mitral annulus and the RV lateral tricuspid annulus.**

Results. **Patients with HCM had a higher blood pressure, septal thickness and LV mass in comparison with the other two groups. The RV wall thickness did not differ between HCM and LVH. The fractional shortening, but not the tricuspid annular plane excursion, was higher in HCM. After adjusting for the mean blood pressure, the Doppler-derived global LV and RV diastolic functions were more impaired in HCM than in LVH. Also the majority of DTI LV and RV diastolic measurements were altered more in HCM. At the RV tricuspid annulus, myocardial diastolic indexes were impaired in HCM and LVH in comparison with controls but the deceleration and relaxation times distinguished also HCM and LVH, being much longer in HCM ($p < 0.0001$). In the overall population, the RV myocardial relaxation time was positively related to the septal wall thickness and the RV wall thickness, even after adjusting for age, heart rate, diastolic blood pressure, fractional shortening and DTI mitral relaxation time.**

Conclusions. **The impairment of RV myocardial relaxation is much more evident in HCM than in LVH, its degree being independently associated with the extent of both the septal and RV wall thickness. Pulsed DTI may be useful to distinguish the extent of RV myocardial dysfunction in different types of cardiac hypertrophy.**

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Introduction

Hypertrophic cardiomyopathy (HCM) is a primary cardiac disease characterized by an increased left ventricular (LV) wall thickness and normal or decreased internal LV cavity dimensions[1]. It is reasonable to suppose that the right ventricle may be involved in this disease, because of an extension of the myopathic process[2] or because of the interposition of hypertrophied interventricular septum which is shared by both ventricles. Right ventricular (RV) diastolic dysfunction has been previously observed[3-5] in HCM. RV involvement may also be expected in arterial systemic hypertension, where both pressure overload and LV mass growth may affect RV function. RV diastolic impairment has been found in arterial systemic hypertension, particularly when associated with LV hypertrophy (LVH)[6-9]. However, little is known about the possible difference between RV function occurring in HCM and that occurring in hypertensive LVH.

While standard echocardiography is widely used to assess the global LV function, this technique does not allow for satisfactory analysis of RV function in HCM and LVH as well as in several other cardiac diseases. This, because of the complexity of the RV geometry which precludes an accurate assessment of the RV internal chamber dimensions and of their changes during the cardiac cycle[10]. The assessment of RV myocardial properties might be, therefore, crucial to better understand the mechanisms underlying the development of RV dysfunction under these circumstances and to detect ear-

ly evidence of the RV involvement associated with these two different types of cardiac hypertrophy. Pulsed Doppler tissue imaging (DTI) has successfully been used to analyze myocardial wall motion abnormalities in different heart diseases[11-15] and it might also be suitable to assess RV regional myocardial changes associated with both HCM and LVH. In a previous report we had investigated the RV myocardial pattern in patients with HCM of the interventricular septum[16]. On these grounds, the present study was designed to compare pulsed DTI myocardial properties of the right ventricle in these two pathologies, in relation to abnormalities of the interventricular septum and of the RV wall as well as to the difference of global RV and LV function.

Methods

Selection of the study population. Having obtained the patients' informed consent and approval of our Institutional Committees, 20 hypertensive patients with LVH, 23 patients affected by LV asymmetric septal HCM, and 30 healthy subjects were enrolled into the study. Hypertensives (diastolic blood pressure ≥ 90 mmHg taken as the mean of three different measurements on three different visits) were considered to have LVH if LV mass index was ≥ 50 g/m$^{2.7}$ (according to the Cornell criteria)[17]. A septal wall thickness ≥ 12 mm was additionally required. The diagnosis of LV HCM was based on echocardiographic evidence of a disproportionate septal wall thickness, in the absence of any identifiable secondary cause of LVH[18]. Exclusion criteria from the study were: diabetes mellitus, coronary artery disease (angina and/or ECG signs of myocardial ischemia), valvular heart disease including any degree of tricuspid regurgitation, NYHA functional classes III and IV, sinus tachycardia, atrial fibrillation, lung disease and pulmonary arterial hypertension (according to the patient's history, physical examination and pulmonary functional tests), inadequate echocardiograms, and the use of cardiac medications. According to the rules of our Institutional Committees, cardiac therapy, if any, was withdrawn in hypertensives and in patients affected by HCM respectively 21 and 2 days before the echocardiograms.

The 20 patients with LVH were selected from a population of 90 subjects with uncomplicated hypertension and referring to the outpatient clinic of the Department of Clinical and Experimental Medicine of the "Federico II" University of Naples (Italy), after excluding 47 patients without LVH, 12 with LVH but a normal septal wall thickness, and 11 with inadequate echocardiograms. Of these patients, 15 were newly diagnosed hypertensives while the other 5 had mild hypertension and had been treated with calcium-channel blockers or diuretics. The 23 patients with HCM (13 with LV outflow tract obstruction according to a gradient ≥ 30 mmHg) were selected from an initial population of 43 consecutive patients referring to the Division of Cardiology of the Monaldi Hospital, after excluding 10 subjects in NYHA classes III-IV, 5 with moderate-severe mitral regurgitation, 3 with chronic atrial fibrillation, and 2 with mild tricuspid regurgitation. Of these patients, 15 were newly diagnosed and the remaining 8 had been treated with beta-blockers or calcium-channel blockers. The 30 healthy subjects were recruited for blood pressure screening from the staff of our institution. The three groups were comparable for sex, age, and heart rate but the body mass index and blood pressure were higher in hypertensives (Table I).

Procedures. Standard Doppler echocardiography and DTI were performed with the subjects in partial left decubitus, using the Vingmed System Five ultrasound system (GE, Horten, Norway) and the Acuson 128 XP10 ultrasound system (Mountain View, CA, USA), both equipped with DTI capabilities. A variable frequency phased-array transducer (2.5-3.5-4.0 MHz) was used for two-dimensional, M-mode and Doppler imaging. Doppler echocardiographic and DTI tracings were recorded on super VHS videotapes and high fidelity paper strip at a velocity of 150 or 100 mm/s. All the measurements were analyzed by two experienced readers and taken as the average of ≥ 3 cardiac cycles, in order to minimize the effect of differences during the breathing cycle.

M-mode LV measurements as well as two-dimensional recognition of the extent and distribution of hy-

Table I. Characteristics of the study population.

Variable	LVH (n = 20)	HCM (n = 23)	Controls (n = 30)
Sex (M/F)	14/6	16/7	21/9
Age (years)	49.8 ± 2.7	45.2 ± 10.6	46.3 ± 5.9
Body mass index (kg/m^2)	28.6 ± 2.4*	25.3 ± 3.6§	23.6 ± 2.4
Heart rate (b/min)	69.0 ± 11.4	75.1 ± 22.2	72.8 ± 10.9
Systolic BP (mmHg)	148.8 ± 9.7**	117.8 ± 16.9§§	125.0 ± 11.2
Diastolic BP (mmHg)	99.0 ± 6.6**	72.6 ± 8.8§§	77.0 ± 6.5
Mean BP (mmHg)	115.6 ± 7.6**	87.7 ± 11.5§§	92.8 ± 8.1

BP = blood pressure; HCM = hypertrophic cardiomyopathy; LVH = left ventricular hypertrophy. * = $p < 0.0001$ LVH vs controls; ** = $p < 0.00001$ LVH vs controls; § = $p < 0.05$ HCM vs LVH; §§ = $p < 0.00001$ HCM vs LVH.

pertrophy were performed in the parasternal short-axis view and using the criteria of the American Society of Echocardiography[19]. Even the RV anterior wall thickness was determined in the parasternal short-axis view. According to the criteria of McKenna et al.[20] for this view, a value ≥ 5 mm for the RV anterior wall was considered the cut-off point for RV hypertrophy. Fractional shortening was calculated as LVIDd - LVIDs/LVIDd × 100, where LVIDd = LV internal end-diastolic diameter and LVIDs = LV internal end-systolic diameter. The LV mass was calculated according to the Penn convention[21] and indexed for body height$^{2.7}$ (Cornell adjustment)[17]. The tricuspid annulus plane systolic excursion was determined by measuring the distance between the tricuspid annulus and RV apex at end-diastole and end-systole of the same cardiac cycle and calculating the difference between these two measurements (in mm)[22] and used as an index of RV systolic function. Pulsed Doppler assessments of the LV and RV inflow were performed in the apical 4-chamber view, with the sample volume placed at the tips level. The following measurements of global LV diastolic function were determined: the E and A peak velocities (m/s) and their ratio, the deceleration time of the E wave (ms), the isovolumic relaxation time (ms, taken as the time interval occurring between the end of the systolic output flow and the transmitral E wave onset, by placing the pulsed Doppler sample volume between the LV outflow tract and the mitral valve)[23]. The following measurements of global RV filling were determined: the E and A peak velocities (m/s), the E/A ratio and the E wave deceleration time[24]. The RV isovolumic relaxation time was measured in the parasternal long-axis view of the RV outflow tract, by determining the interval from the end of pulmonary outflow to the onset of tricuspid inflow. Our methods and reproducibility in measuring Doppler indexes were previously reported[25].

DTI was performed using transducer frequencies of 3.5-4.0 MHz, adjusting the spectral pulsed Doppler signal filters to obtain the Nyquist limit of 15 and 20 cm/s and using the minimal optimal gain. In the apical 4-chamber view, the pulsed Doppler sample volume was subsequently placed at the level of the LV lateral mitral annulus and the RV lateral tricuspid annulus. The apical 4-chamber view was chosen to obtain a quantitative assessment of the regional wall motion almost simultaneous to the Doppler RV and LV inflow and to minimize the incidence angle between the Doppler beam and longitudinal ventricular motion. Schema of the DTI pattern, characterized by a myocardial systolic wave (S_m) and two diastolic waves – early (E_m) and atrial (A_m) – and measurement methodology are depicted in figure 1. The following measurements were determined in each region as indexes of regional function: myocardial peak velocity of the S_m (m/s), pre-contraction time (from the onset of the ECG QRS complex to the beginning of the S_m), and contraction time (from the beginning to the end of the S_m) (all in ms) as systolic indexes,

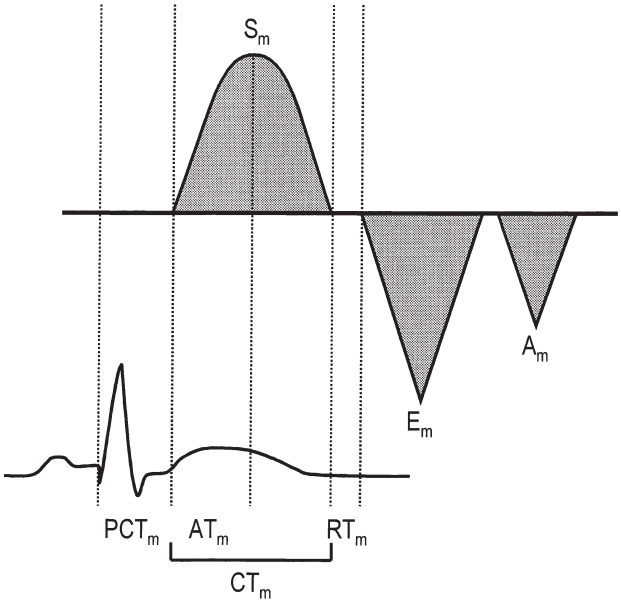

Figure 1. *Schema of a normal right ventricular Doppler tissue imaging pattern characterized by a myocardial systolic wave (S_m) and two diastolic waves – early (E_m) and atrial (A_m). CT_m = myocardial contraction time; PCT_m = myocardial pre-contraction time; RT_m = myocardial relaxation time.*

E_m and A_m peak velocities (m/s), E_m/A_m ratio, myocardial deceleration time of the E_m velocity (DT_m, ms), and RT_m (ms) – as the time interval occurring between the end of the S_m and the onset of the E_m – as diastolic measurements. DTI methods and the reproducibility in our laboratories were previously described[26].

Statistical analysis. Statistical analyses were performed by using the SPSS/PC for Windows release 6.0 statistical package (Chicago, IL, USA). Variables are presented as mean ± 1 SD. Analyses of variance (ANOVA) by the Scheffè *post-hoc* test for multiple comparisons were performed to estimate the intergroup difference of clinical characteristics and of the echocardiographic evaluation of both ventricles. Because of a significant blood pressure difference, the intergroup comparison of Doppler and DTI data was performed by MANOVA, that is by analysis of covariance and adjusting the assessed variables for the mean blood pressure. Linear regression analyses and a partial correlation test by Pearson's method were used to assess univariate relations. Stepwise, forward, multiple regression analyses were performed to weigh the independent effects of potential determinants on a dependent variable. The null hypothesis was rejected for $p < 0.05$.

Results

Doppler echocardiographic analysis of the left and right ventricles. Echocardiographic analyses of the left and right ventricles are listed in table II. The septal thickness and LV mass index were higher in HCM. The

Table II. Echocardiographic measurements of the left and right ventricles.

Variable	LVH	HCM	Controls
Left ventricle			
IVST (mm)	12.6 ± 0.7****	20.7 ± 4.0§§††	8.8 ± 1.4
PWT (mm)	9.4 ± 1.5***	10.1 ± 1.2§§	7.6 ± 1.3
LVIDd (mm)	53.3 ± 4.1	44.5 ± 5.2§§††	50.8 ± 4.2
LVIDs (mm)	36.2 ± 3.6	26.1 ± 4.7§§††	34.5 ± 3.5
Endocardial FS (%)	31.7 ± 3.9	41.3 ± 7.3§§††	31.8 ± 4.9
Relative wall thickness	0.41 ± 0.04***	0.66 ± 0.12§§††	0.34 ± 0.07
LV mass	256.8 ± 59.4****	323.9 ± 92.2§§†	158.4 ± 35.6
LV mass index (g/m$^{2.7}$)	63.2 ± 6.8***	91.2 ± 26.9§§†	39.1 ± 18.0
Right ventricle			
RV wall thickness (mm)	4.6 ± 0.8*	4.6 ± 1.2§	4.0 ± 0.6
TAPSE (mm)	17.5 ± 2.9	18.7 ± 3.3	18.6 ± 3.4

FS = fractional shortening; IVST = interventricular septal thickness; LV = left ventricular; LVIDd = LV internal diastolic dimensions; LVIDs = LV internal systolic dimensions; PWT = posterior wall thickness; TAPSE = tricuspid annulus plane systolic excursion. Other abbreviations as in table I. * = $p < 0.01$, ** = $p < 0.001$, *** = $p < 0.0001$, **** = $p < 0.00001$ LVH vs controls; § = $p < 0.05$, §§ = $p < 0.00001$ HCM vs controls; † = $p < 0.001$, †† = $p < 0.00001$ HCM vs LVH.

RV anterior wall thickness was not different between HCM and LVH but the prevalence of RV hypertrophy (i.e., RV anterior wall thickness ≥ 5 mm[19]) was 47% (10/23) in HCM and 35% (7/20) in LVH ($p < 0.01$). LV fractional shortening was greater in HCM while the tricuspid annulus plane systolic excursion did not differ among the three groups. In table III, the standard Doppler-derived mitral and tricuspid inflow diastolic assessments (adjusted for mean blood pressure) are presented. Except for the E/A ratio, all LV and RV diastolic indexes were more impaired in HCM than in LVH.

Doppler tissue imaging evaluation of the left ventricular mitral annulus and of the right ventricular tricuspid annulus. DTI analyses of the LV lateral mitral annulus and of the RV lateral tricuspid annulus (adjusted for mean blood pressure) are summarized in table IV. At the LV mitral annulus, myocardial systolic indexes did not differ among the three groups while the majority of myocardial diastolic measurements were significantly changed in both diseases compared to controls and were much more altered in HCM than in LVH. At the RV tricuspid annulus, in the presence of a mild S_m increase in HCM, the E_m/A_m ratio was similar between LVH and HCM but the DT_m and RT_m were longer (both $p < 0.001$) in HCM than in LVH. Of note, the RV RT_m was absent (i.e., 0 ms) in 14/30 (46.7%) healthy subjects, in 3/20 (15%) patients with LVH but in none of the HCM patients. Figure 2 displays the DTI patterns in LVH and HCM respectively: it may be seen that the E_m/A_m ratio is < 1 in both groups of patients but the RT_m is mildly longer in patients with LVH and much more prolonged in patients with HCM.

Relationships between variables. In the overall population, the following relations between the Doppler LV and RV inflow measurements were observed: E and A peak velocities, both $r = 0.31$ ($p < 0.01$); E/A velocity ratio $r = 0.34$ ($p < 0.005$), E wave deceleration time r =

Table III. Standard Doppler measurements of the left and right ventricles (adjusted for mean blood pressure).

Variable	LVH	HCM	Controls
Left ventricle			
Peak velocity E (m/s)	0.59 ± 0.19**	0.78 ± 0.22††	0.79 ± 0.10
Peak velocity A (m/s)	0.58 ± 0.16*	0.76 ± 0.24§§††	0.64 ± 0.11
Peak velocity E/A	1.03 ± 0.25*	1.04 ± 0.35§§	1.24 ± 0.26
Deceleration time (ms)	201.1 ± 20.0**	268.7 ± 29.0§§§†††	156.2 ± 28.0
IVRT (ms)	82.6 ± 12.0	110.1 ± 8.6§§††	84.0 ± 15.0
Right ventricle			
Peak velocity E (m/s)	0.46 ± 0.15**	0.57 ± 0.15§†	0.68 ± 0.16
Peak velocity A (m/s)	0.44 ± 0.14	0.55 ± 0.16†	0.51 ± 0.15
Peak velocity E/A	1.06 ± 0.24**	1.07 ± 0.25§§	1.37 ± 0.32
Deceleration time (ms)	191.8 ± 37.0**	281.3 ± 41.2§§§††	159.7 ± 42.2
IVRT (ms)	78.9 ± 14.5**	107.9 ± 9.6§§††	81.5 ± 18.1

IVRT = isovolumic relaxation time. Other abbreviations as in table I. * = $p < 0.001$, ** = $p < 0.0001$ LVH vs controls; § = $p < 0.01$, §§ = $p < 0.001$, §§§ = $p < 0.0001$ HCM vs controls; † = $p < 0.01$, †† = $p < 0.001$ HCM vs LVH.

Table IV. Pulsed Doppler tissue imaging of the left ventricular mitral annulus and of the right ventricular tricuspid annulus (adjusted for mean blood pressure).

Variable	LVH	HCM	Controls
LV mitral annulus			
S_m peak velocity (m/s)	0.06 ± 0.02	0.08 ± 0.05	0.07 ± 0.01
PCT_m (ms)	88.7 ± 21.8	92.4 ± 22.8	90.6 ± 15.0
CT_m (ms)	271.6 ± 30.2	278.8 ± 32.9	276.2 ± 31.0
E_m peak velocity (m/s)	0.09 ± 0.02*	0.08 ± 0.03§	0.12 ± 0.05
A_m peak velocity (m/s)	0.09 ± 0.03	0.11 ± 0.04§†	0.09 ± 0.03
E_m/A_m peak ratio	1.00 ± 0.25**	0.73 ± 0.25§§§††	1.33 ± 0.50
DT_m (ms)	110.9 ± 46.2*	176.5 ± 54.1§§§†††	102.7 ± 25.1
RT_m (ms)	94.5 ± 23.1**	158.9 ± 57.0§§§†††	78.3 ± 22.0
RV tricuspid annulus			
S_m peak velocity (m/s)	0.14 ± 0.04	0.17 ± 0.04†	0.16 ± 0.09
PCT_m (ms)	89.4 ± 26.1	94.0 ± 29.0	92.7 ± 25.0
CT_m (ms)	275.5 ± 33.0	280.4 ± 30.2	276.1 ± 35.0
E_m peak velocity (m/s)	0.12 ± 0.03	0.17 ± 0.05†	0.17 ± 0.08
A_m peak velocity (m/s)	0.14 ± 0.05	0.20 ± 0.09§†	0.15 ± 0.08
E_m/A_m peak ratio	0.86 ± 0.30**	0.85 ± 0.42§§	1.13 ± 0.35
DT_m (ms)	124.3 ± 60.0**	199.8 ± 70.0§§§†††	114.0 ± 38.0
RT_m (ms)	40.6 ± 30.0***	120.3 ± 36.1§§§†††	10.0 ± 21.0

A_m = myocardial atrial wave; CT_m = myocardial contraction time; DT_m = myocardial deceleration time; E_m = myocardial early wave; LV = left ventricular; PCT_m = myocardial pre-contraction time; RT_m = myocardial relaxation time; RV = right ventricular; S_m = myocardial systolic wave. Other abbreviations as in table I. * = $p < 0.01$, ** = $p < 0.001$, *** = $p < 0.0001$ LVH vs controls; § = $p < 0.01$, §§ = $p < 0.001$, §§§ = $p < 0.0001$ HCM vs controls; † = $p < 0.01$, †† = $p < 0.001$, ††† = $p < 0.0001$ HCM vs LVH.

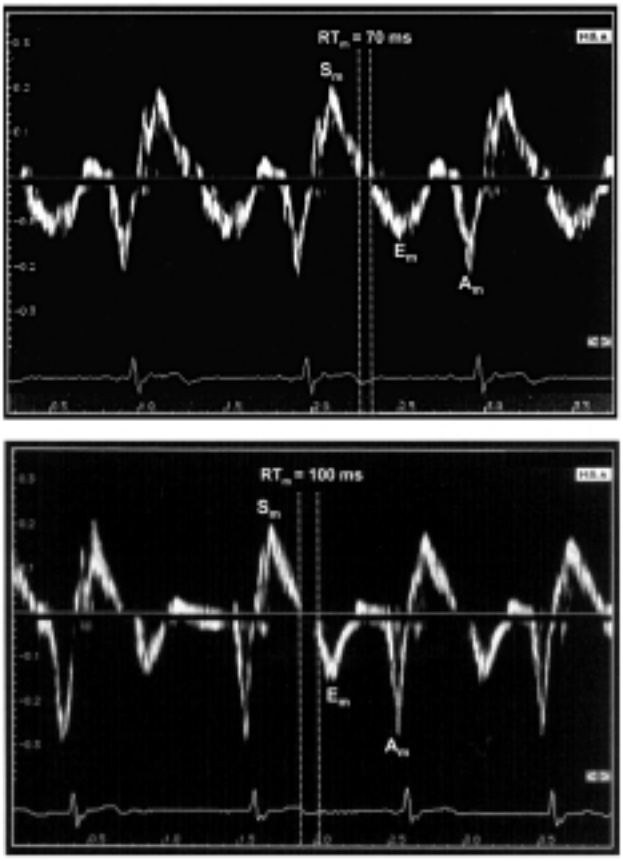

Figure 2. *Doppler tissue imaging patterns of the tricuspid annulus in a hypertensive patient with left ventricular hypertrophy* (upper panel) *and in a patient with hypertrophic cardiomyopathy* (lower panel) *respectively: the E_m/A_m ratio is < 1 at both levels while the RT_m is 70 ms in the patient with left ventricular hypertrophy and 100 ms in the patient with hypertrophic cardiomyopathy. Abbreviations as in figure 1.*

0.39 ($p < 0.001$), isovolumic relaxation time r = 0.37 ($p < 0.001$). There was no relationship between LV fractional shortening and the tricuspid annulus plane systolic excursion. In the overall population, we also found the following significant univariate relations between DTI measurements of the LV mitral annulus and of the RV tricuspid annulus: peak S_m r = 0.35 ($p < 0.005$); peak E_m r = 0.43 ($p < 0.0002$); peak A_m r = 0.46 ($p < 0.0001$); peak E_m/A_m ratio r = 0.36 ($p < 0.001$); DT_m r = 0.49 ($p < 0.00001$); and RT_m r = 0.60 ($p < 0.00001$). Among RV DTI measurements, the RV E_m/A_m ratio and the DT_m were significantly related to the septal wall thickness (r = -0.29, $p < 0.01$, and r = 0.37, $p < 0.002$ respectively) but not to the RV wall thickness. The RV RT_m was associated with both the septal wall thickness ($r = 0.70$, $p < 0.00001$) and the RV wall thickness (r = 0.36, $p < 0.001$) (Fig. 3). Of note, these last two relations were not significant when analyzed separately in the three assessed groups. The RV RT_m was also related to diastolic blood pressure (r = 0.29), heart rate (r = -0.31), and age (r = 0.30) (all $p < 0.01$).

In a stepwise forward, multiple linear regression analysis including age, heart rate, mean blood pressure, LV fractional shortening and LV mitral RT_m as potential confounders, the septal wall thickness (standardized β coefficient 0.74, $p < 0.00001$) and the RV wall thickness (standardized β coefficient 0.22, $p < 0.01$) were the only independent predictors of the RV RT_m (cumulative r^2 = 0.60, SE 35.8 ms, $p < 0.0001$). After removing the effects of the septal wall thickness and of the RV wall thickness, the partial correlation coefficients for the other variables versus RV RT_m were not significant.

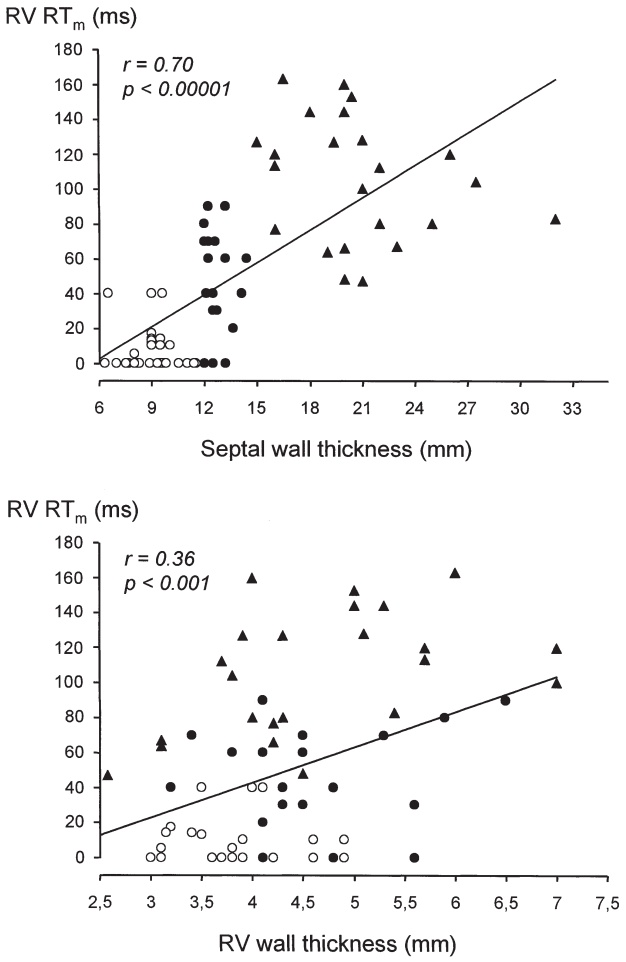

Figure 3. *Scatter plots and regression line of the right ventricular (RV) myocardial relaxation time (RT_m) with both the septal wall thickness* (upper panel) *and the RV anterior wall* (lower panel) *in the overall population.* Open circles: *controls;* filled circles: *hypertensives with left ventricular hypertrophy;* triangles: *patients with hypertrophic cardiomyopathy.*

Discussion

Abnormalities of RV diastolic filling were described in HCM[3-5] as well as in hypertensive LVH[6-9]. We already observed the DTI pattern of hypertrophic and thin LV walls in LVH[15] and also in LV HCM involving the septal wall[14]. The present study shows the usefulness of pulsed DTI to distinguish the degree of RV myocardial involvement in these two different types of cardiac hypertrophy.

Right ventricular chamber function. In the present study, the RV global systolic function was assessed by the tricuspid annulus plane systolic excursion, a reliable measurement of RV longitudinal systolic motion[22]. Tricuspid annulus plane systolic excursion was similar in HCM, LVH and controls. The RV systolic function had not been explored enough in HCM while a reduction in the radionuclide angiographic RV ejection fraction had been found in hypertensives, being also associated with higher atrial and RV end-diastolic pressures[27]. Similar changes might not be expected in our population where congestive heart failure was an exclusion criterion. We also confirmed RV diastolic dysfunction in hypertensives[6-9] and, to a greater extent, in HCM[3-5].

Right ventricular myocardial function. RV pulsed DTI has recently been investigated in a healthy population[28] and in patients with heart failure[29] while in a previous study, we found DTI-derived RV myocardial diastolic dysfunction in the septal wall of HCM patients[16]. To our knowledge, this is the first study comparing the RV myocardial motion between HCM and hypertensive LVH by this technique. The RV E_m/A_m ratio impairment, the prolongation of the RV DT_m and, above all, of the RT_m were evident in both diseases but the changes of the DT_m and RT_m were prominent in HCM.

Pulsed DTI estimates myocardial wall velocities and, because of its high temporal resolution[13], also the time intervals throughout the cardiac cycle. The RV RT_m reflects the energy-dependent phase of isometric relaxation occurring between pulmonary valve closure and tricuspid valve opening (i.e., in constant RV volume conditions) while the E_m/A_m ratio expresses RV passive myocardial diastolic properties. Because RV tricuspid DTI velocities are preload independent[30], a RV tricuspid E_m/A_m ratio < 1 is significantly more indicative of a myocardial passive diastolic impairment than the reversal of the RV inflow E/A ratio which is affected by several confounders[24]. In the present study, the RV RT_m was much more longer in HCM, its mean value being more than twice that observed in the LVH group. RV myocardial active relaxation is extremely short or even absent in healthy subjects (it also occurred in 46.7% of our control group) whereas it is increased in several RV pathologies[10]. Experimental studies have reported that the right ventricle, unlike the left ventricle, starts its diastolic filling without an isovolumic relaxation interval[31-33] since it works against a lower vascular impedance. Abnormalities of RV myocardial relaxation in HCM might be mainly due to an extension of the myopathic process to walls other than the interventricular septum[34,35] and we already demonstrated RV tricuspid RT_m lengthening in septal HCM[16]. Possible mechanisms of impaired RV isovolumic relaxation in arterial systemic hypertension involve both a pulmonary afterload increase[36] as well as RV hypertrophy developing hand in hand with LVH[37,38]. RV RT_m prolongation has been observed in patients with pulmonary hypertension (non invasively estimated)[39] who, however, were excluded by selection in the present study. On the other hand, the absence of an RT_m in some hypertensives may be possibly explained on the basis of younger age or of a not very long hypertensive history.

Association between right ventricular and left ventricular Doppler tissue imaging indexes. In accordance with studies showing an association between the

RV and LV diastolic inflows in arterial hypertension[6-9] (also found in the present study), DTI-derived RV diastolic measurements were closely related to the homologous indexes of the LV mitral annulus. A significant association was also observed between the RV tricuspid systolic peak velocity and that of the LV mitral annulus. These data may suggest a functional interaction between the two ventricles under these circumstances. Ventricular interdependence occurs because of the close association between the two ventricles which share myocardial fibers and the septal wall and are both enclosed within the pericardium[10].

Association of right ventricular RT_m with septal and right ventricular wall thickness. In the present study, the lengthening of the RV tricuspid RT_m was related positively to the septal thickness and, to a lesser extent, to the RV anterior wall thickness which was similarly greater in both HCM and LVH than in controls. Interestingly, these associations were significant in the overall population but not in the three separate groups, underscoring an interesting association between the increasing wall thickness delimiting the right ventricle and the alterations in RV relaxation, independently of the underlying LV disease. Multiple linear regression analysis provided additional information about these associations. In this model, the normalization for age and heart rate was needed because of their recognized influence on diastolic function[40,41]. The adjustment for mean blood pressure was done because of its higher value in hypertensives with LVH, the degree of LV afterload being associated with the rate of RV relaxation[42]. Even the LV fractional shortening was included as a potential confounder since it was greater in HCM (as previously described for early stages of this disease[43]). Similarly, the LV mitral RT_m was included in view of the possible ventricular interaction underscored by the univariate relations between the LV and RV DTIs. After adjusting for these variables, the septal thickness mainly and, to a lesser extent, the RV wall thickness were independent contributors of the RT_m, together justifying 58% of its variation in the overall population.

An association between the septal wall thickness and the RV myocardial diastolic measurements might be expected in a population with different degrees of septal hypertrophy as that presented by patients with LVH and HCM. Pathologic hypertrophy is associated with myocardial fibrosis which is a main determinant of abnormal myocardial relaxation[44]. Even the association between the RV anterior wall thickness and the degree of RT_m lengthening was not unexpected. Habib and Zoghbi[7] found a significant association between the RV wall thickness and RV filling measurements in systemic arterial hypertension. A RV wall thickness increase has been found in uncomplicated systemic arterial hypertension[37,38] while McKenna et al.[20] observed a high prevalence (44%) of RV hypertrophy in LV HCM. We found a similar prevalence of RV hypertrophy (47%) in HCM while it was lower (35%) in LVH.

Study limitations. The main study limitation is the lack of hemodynamic data. An assessment by RV heart catheterization might have provided more accurate information about RV and right atrial pressures as well as about pulmonary arteriolar resistance. However, RV hypertrophy has not been found to be associated with the occurrence of pulmonary arterial hypertension in patients with HCM[20]. In addition, our selection criteria excluded those patients with any degree of pulmonary arterial hypertension. Another limitation is that we measured the RV wall thickness only in the parasternal view. McKenna et al.[20] demonstrated that only the use of at least four measurements taken in multiple views (parasternal, apical and subcostal approaches) allows accurate estimation of RV hypertrophy in LV HCM. An underestimation of the RV wall thickness might, however, have blunted the observed impact of the RV wall increase on the RV RT_m prolongation in HCM. Furthermore, in the present study the prevalence of RV hypertrophy in HCM was similar to that observed by McKenna et al.[20] themselves. Finally, our findings may not be extrapolated to the overall population of patients with HCM because of the exclusion of severe heart failure which may have eliminated patients with advanced systolic impairment. However, we intentionally selected relatively asymptomatic patients to examine early the variations in DTI regional diastolic properties in HCM.

In conclusion, the present study shows the additional usefulness of pulsed DTI to detect different degrees of RV myocardial diastolic dysfunction in HCM and in hypertensive LVH. RV myocardial diastolic changes develop both in HCM and LVH but abnormalities of myocardial relaxation are much more evident in HCM. These abnormalities may be due to multiple factors including ventricular interdependence and loading conditions. However, based on the independent associations found between the degree of prolongation in RV myocardial relaxation and the magnitude of the increase in both the septal and RV anterior wall thickness, the hypertrophy of the walls delimiting the RV chamber appears as the main determinant of impaired RV relaxation developing in different types of cardiac hypertrophy.

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