

Cardiac Magnetic Resonance with Delayed Enhancement of the Right Ventricle in patients with Left Ventricle primary involvement: diagnosis and evaluation of functional parameters.

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Abstract. Cardiac Magnetic Resonance (CMR) allows an accurate Right Ventricle (RV) assessment that could be of great relevance in diseases causing inflammation or fibrosis. The aim of this study was to evaluate the concomitant involvement of the RV in patients with delayed enhancement (DE) of the Left Ventricle (LV-DE) using CMR. We retrospectively enrolled 95 (male n. 66; age 55±18years; BMI 26±5kg/m²) consecutive patients with LV-DE who underwent a CMR (Achieva 1.5 T, Philips) for different indications: post-ischemic dilated cardiopathy (PDM), hypertrophic cardiomyopathy (HCM), myocardial infarction (MI), myocarditis/pericarditis (MP) and congenital heart disease (CD). We assessed the presence and extension of DE and functional parameters such as ventricular end-diastolic (EDV), end-systolic volumes (ESV) and ejection fraction (EF) of both LV and RV. Prevalence of RV-DE was 30.5% (29/95): 75% (3/4) for CD, 44% (4/9) for PDM, 36% (17/47) for MI, 27.8% (5/18) for MP and 0% (0/17) for HCM. LV-EF and RV-EF were 53±15mL and 51±13mL, respectively, for patients without RV-DE (RV-DE-), and 40±19 mL and 42±15 mL, respectively, for patients with RV-DE (RV-DE+) ($p<0.05$), while LV-EDV and LV-ESV were 80±28 mL and 40±26 mL, respectively, for RV-DE- and 100±45 mL and 65±49 mL, respectively, for RV-DE+ ($p<0.05$). The prevalence of RV-DE in patients with LV primary involvement is not negligible and it is found mainly in patients with CD and PDM and then in patients with MI and MP. It is more often associated with LV-EF and RV-EF reduction and increase in LV volumes. (www.actabiomedica.it)

Key words: Cardiac Magnetic Resonance; Delayed Enhancement; Right Ventricle; Left Ventricle; Cardiomyopathies

Introduction

The Right Ventricle (RV) is a cardiac chamber difficult to assess, and, even though the left ventricle (LV) is considered more important, it plays a crucial role in cardiac and pulmonary physiology. RV can be involved in different pathologic conditions such as myocardial infarction (MI) (anterior, inferior or isolated right ventricular MI), hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy, myocarditis/pericarditis (MP), pulmonary hypertension and congenital heart disease (CD). RV free wall measures about 3 mm, the thickness and the complex geometry make RV abnormalities less common than left LV diseases with a lack of understanding of the normal and diseased state of the RV(1,2). RV involvement can be underestimated because of echocardiography limited role in its evaluation when compared with the assessment of LV(3). Cardiac Magnetic Resonance (CMR) is a three-dimensional imaging modality that allows

carditis (MP), pulmonary hypertension and congenital heart disease (CD). RV free wall measures about 3 mm, the thickness and the complex geometry make RV abnormalities less common than left LV diseases with a lack of understanding of the normal and diseased state of the RV(1,2). RV involvement can be underestimated because of echocardiography limited role in its evaluation when compared with the assessment of LV(3). Cardiac Magnetic Resonance (CMR) is a three-dimensional imaging modality that allows

the assessment of multiple different parameters of cardiovascular anatomy and function(4-6).

CMR can define cardiac anatomy and structure, characterizing tissue composition and myocardial fibrosis by means of delayed enhancement (DE). All these CMR features are helpful in patients with acoustic window limitations at transthoracic echocardiography evaluation(7). Often, when dealing with diseases causing inflammation and/or fibrosis of the LV, we tend to overlook RV involvement so leading to inaccuracies that may affect the diagnostic and, even more, the prognostic evaluation(8). For instance, RV involvement in ST-segment elevation MI is detected more frequently with CMR than other techniques such as electrocardiogram (ECG) or echocardiography and it represents an independent prognostic indicator of Major Cardiac Adverse Cardiac Events (MACE)(9). The aim of our study is to evaluate the concomitant involvement of the RV in patients with LV-DE using CMR.

Methods

Over a period of 6 months we enrolled 95 consecutive patients (male/female 66/29; age 54.4 ± 18.2 years; BMI 25.5 ± 4.6 kg/m²) who underwent a CMR (Achieva 1.5T, Philips) for different indications such as post-ischemic dilated cardiomyopathy (PDM), HCM, MI, MP and CD. A complete clinical file including demographics, cardiovascular risk factors and symptoms was recorded. Inclusion criterium was the presence of LV-DE after gadolinium injection. Exclusion criteria were aortocoronary bypass and Left Bundle Branch Block (LBBB). Informed consent was waived by the IRB due to the retrospective nature of the study.

ECG

All patients underwent a standard 12 lead ECG. We considered myocardial infarction as a ST elevation in the absence of LV hypertrophy or LBBB as follows:

a new ST elevation at the J point in at least 2 contiguous leads of 2 mm (0.2 mV) in men or 1.5 mm (0.15 mV) in women in leads V₂-V₃ and/or of 1 mm (0.1 mV) in other contiguous chest leads or the limb leads(10, 11).

CMR

All CMR exams were performed with a 1.5 Tesla MR scanners (Achieva; Philips Medical System), with a dedicated eight-element phased-array cardiac synergy coil for signal reception with a cardiac-respiratory gating. The standard CMR protocol included a 2D cine balanced steady-state free-precession sequences (cine bSSFP) and a contrast-enhanced inversion recovery segmented gradient echo sequence (IR-Flash) acquired 7-8 minutes after the intravenous administration of 0.2 mmol/kg gadobenate dimeglumine (Gd-BOPTA; MultiHance, Bracco) for DE evaluation. 2D cine b-SSFP short axis sequences were performed for both ventricles with the following parameters: TR 3.1 ms, TE 1.53 ms; flip angle 60°; bandwidth 1249.7 HZ/pixel; in plane resolution 2x2.3 mm; slice thickness 8 mm; interslice gap 2 mm; temporal resolution 31.52 ± 5.93 ms (according to cardiac frequency); 30 cardiac phases; SENSE off; Half scan on. IR-FLAH sequences were acquired into three cardiac planes (long axis, short axis and 4-chamber), with the following parameters: TR 8 ms, TE 4 ms; flip angle 25°; bandwidth 1249.7 HZ/pixel; resolution in plane 1.4x1.4 mm²; slice thickness 6 mm without gap inter-slice. Inversion time (TI) was manually adjusted from 200 to 260 ms to obtain optimal myocardial nulling of remote LV myocardial tissue. In case of RV-DE suspicion, TI was adjusted separately in order to obtain remote right and left ventricle nulling.

Image analysis

Data were transferred to a dedicated analysis workstation equipped with a quantitative semi-automatic software for volume analysis (Argus, Siemens Medical Solution). Biventricular functional evaluation was realized "in consensus" by two operators and included end-diastolic volume (EDV), end-systolic volume (ESV), ejection fraction (EF), LV mass, stroke volume (SV). All CMR images were analysed in consensus by two trained operators evaluating DE pattern and localization for each patient.

RV myocardium was divided into three parts corresponding to free wall, interventricular septum and right ventricular junction to ventricular septum, re-

Table 1. Demographics.

Parameter	Population (n=95)	RV DE + (n=29)	RV DE - (n=66)	p
Age (years) (mean±SD)	54.4±18.2	59.2±16	52.2±18.8	>0.05
Male gender (%)	66 (69%)	23 (79%)	43 (65%)	>0.05
Weight (Kg)	72.7±14.1	71.7±13.7	73±14.4	>0.05
Height (m)	1.7±0.1	1.7±0.1	1.7±0.1	>0.05
BMI (kg/m ² ; mean±SD)	25.5±4.6	25±4.1	25.7±4.8	>0.05
Family history (%)	39 (41%)	12 (41%)	27 (41%)	>0.05
Smoking (%)	28 (29%)	9 (31%)	19 (29%)	>0.05
Hypertension (%)	48 (51%)	13 (45%)	35 (53%)	>0.05
Dyslipidemia (%)	35 (37%)	8 (28%)	27 (41%)	>0.05
Obesity	18 (19%)	3 (10%)	15 (23%)	>0.05
Symptoms	59 (62%)	16 (55%)	43 (65%)	>0.05

Abbreviations: SD: standard deviation; BMI, body mass index

spectively. Right ventricle involvement was defined as the presence of RV-DE defined as a visually hyper-enhanced myocardium compared to remote normal myocardium in the IR-Flash sequences acquired 7-8 minutes after gadolinium chelates injection. Moreover, RV-DE had to be confirmed in two adjacent short-axis images or in one short-axis image and a long-axis image at a corresponding location in order to avoid misinterpretation due to artefacts, morphological variations or septal clefts(12).

Statistical Analysis

Normally distributed variables are presented as mean±SD. Absolute values and percentages were calculated to describe the population. Differences between groups were assessed by the t-Student test for continuous data with normal distribution and homogeneity of variance and with the Mann-Whitney test for the significance of difference between the distributions of two independent samples for non-parametric statistical hypothesis. A p-value of 0.05 was set for statistical significance.

Results

We divided the population into patients with RV-DE (RV-DE+) and patients without RV-DE (RV-DE-). The two subgroups were comparable for age,

gender, weight, height, BMI, risk factors and symptoms (p>0.05) (Table 1).

According to clinical files, ECG results and CMR DE images, we found: 9 patients (9.5%) with DCM, 18 (19%) with MP, 47 (49.5%) with a MI, 17 (18%) with HCM and 4 (4%) with CD (Table 2 and Figure 1). Functional parameters (EDV, ESV and EF) of the two populations are shown in Table 3 and Figure 4. RV-DE was present in 29 patients: 3 (10%) patients affected by CD, 4 (14%) patients with DCM, 5 (17%) with MP and 17 (59%) with ischemic heart disease (Table 3). RV-DE+ patients had a significant lower LV-EF (40.3% vs. 52.5%, p<0.05) and RV-EF (42.1% vs. 50.5%, p<0.05) and a higher LV-EDV (100.7 mL vs. 80.2 mL, p<0.05). Functional parameters in different subgroups are shown in Tables 4 and Figures 5. RV-DE + patients with a DCM or MI showed a reduced cardiac function with a lower biventricular EF together with a biven-

Table 2. CMR indications.

Indications	Prevalence n. (%)
Congenital Diseases (%)	4 (4%)
Dilated cardiomyopathy (%)	9 (9%)
Hypertrophic cardiomyopathy (%)	17 (18%)
Mio/pericarditis (%)	18 (19%)
Acute ischemic heart disease (%)	32 (34%)
Chronic ischemic heart disease (%)	15 (16%)
TOTAL	95 (100%)

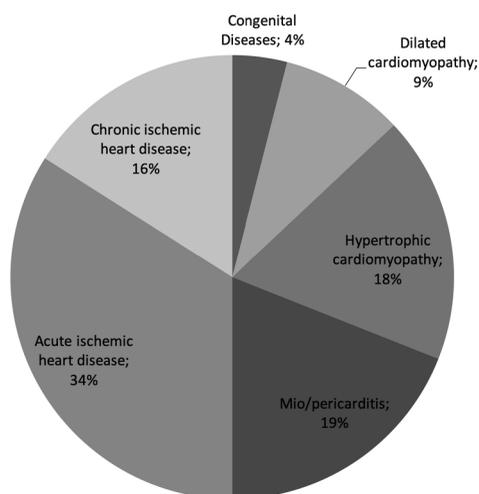


Figure 1. Distribution of indications for CMR. The Figure shows the distribution of CMR indication in our population of study.

tricular dilatation as compared to RV-DE- patients. No patient with HCM showed RV-DE. Within patients with MP, 5 presented RV involvement: 4 patients presented free wall involvement and only one patient had also interventricular septum DE. Within patients with MI, RV-DE was found in 17 patients that presented a heterogeneous distribution without a specific topographic localization.

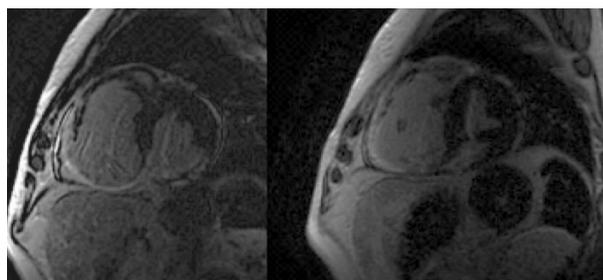


Figure 2. Delayed enhancement of right and left ventricle. The figure shows a short axis acquisition with delayed enhancement of right and left ventricular wall with a subendocardial and transmural extension (ischemic pattern) in a patient with a previous myocardial infarction.

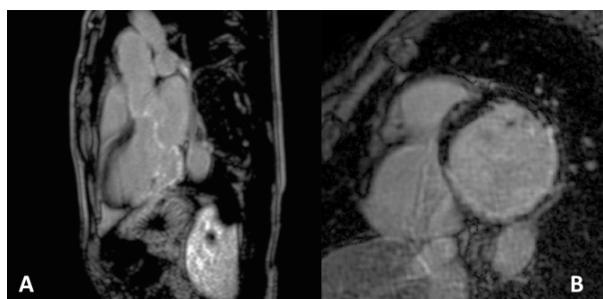


Figure 3. Delayed enhancement of left ventricle. The figure shows the presence of delayed enhancement (ischemic pattern) in a patient with a myocardial infarction without right ventricular involvement. A. The radial acquisition shows delayed enhancement of the inferior wall. B. The short axis shows subendocardial delayed enhancement of the inferior septum, inferior wall and lateral wall.

Table 3. Functional Parameters and Distribution of CMR Indications.

Functional Parameters (mean±SD)	Population	RV DE+ (n=29)	RV DE- (n=66)	p
LV				
EF (%)	48.8±17.2	40.3±18.5	52.5±15.3	<0.05
SV (ml)	38.3±12.4	34.9±13.6	39.8±11.7	<0.05
EDV (ml)	86.5±35.4	100.7±45.6	80.2±28	<0.05
ESV (ml)	48.2±36.9	65.8±49.3	40.4±26.9	<0.05
RV				
EF (%)	48.1±13.9	42.1±14.6	50.5±13	<0.05
SV (ml)	37.9±11.9	33.5±11.7	39.8±11.6	<0.05
EDV (ml)	81.4±20.7	83.4±21.2	80.6±20.6	>0.05
ESV (ml)	45.4±20.6	51.9±22.9	42.6±19	0.05
CMR indications				
CD (n.)	4	3	1	Na
DCM (n.)	9	4	5	Na
HCM (n.)	17	0	17	Na
MP (n.)	18	5	13	Na
MI (Acute & Chronic) (n.)	47	17	30	Na

The Table shows in the Upper Panel functional parameters of the whole population and of the two subgroups (RV DE+ and RV DE-). The Lower Panel shows CMR indications of the whole population and of the two subgroups (RV DE+ and RV DE-).

Abbreviations: ml: milliliters; n.: number; SD: standard deviation; EF: Ejection Fraction; SV: Stroke Volume; EDV: End-Diastolic Volume; ESV: End-Systolic Volume; CD: congenital disease. DCM: dilated cardiomyopathy; HCM: hypertrophic cardiomyopathy; MP: myocarditis/pericarditis; MI: myocardial infarction.

Table 4. Functional parameters in different subgroups.

Parameters		DCM		MI		MP	
		DE+ (n=4)	DE- (n=5)	DE+ (n=17)	DE- (n=30)	DE+ (n=5)	DE- (n=13)
LV	EF	17.8 ±9.4	40.4±13.9	39.2±17.2	49.4±17.2	57±11.2	54.5±9.9
	SV	21.5±3.1	43.4±9.6	36.3±15.8	36.8±11.6	39±4.1	40.5±12.1
	EDV	137.3±49.7	116±47.6	104.6±48.3	80.6±29.6	69.8±10.4	74.1±16.8
	ESV	115.8±50.6	72.6±45.7	68.3±50.4	43.9±30.4	31±13	33.5±8.9
RV	EF	22.8 ±6.7	49±11.2	45.6±14.7	48.3±14.1	48.2±7.8	45.5±6.6
	SV	21.5±3.1	43.4±9.6	33.9±13.1	36.7±11.4	39±4.1	40.5±12.1
	EDV	97.5±17.7	89.2±7.9	78.5±23.1	78.2±22.4	81.8±7.8	88.4±20.6
	ESV	75.8±18.5	45.8±11.5	48.2±24.4	45.5±23.4	42.6±9.3	47.8±10.9

The table shows biventricular functional parameters of the different subgroups: patients with DCM, MI and MP. Values are presented as mean±SD.

Abbreviations: DCM = dilated cardiomyopathy; MI = myocardial infarction; MP = myocarditis/pericarditis; SD = standard deviation; EF = Ejection Fraction; SV = Stroke Volume; EDV = End-Diastolic Volume; ESV = End-Systolic Volume.

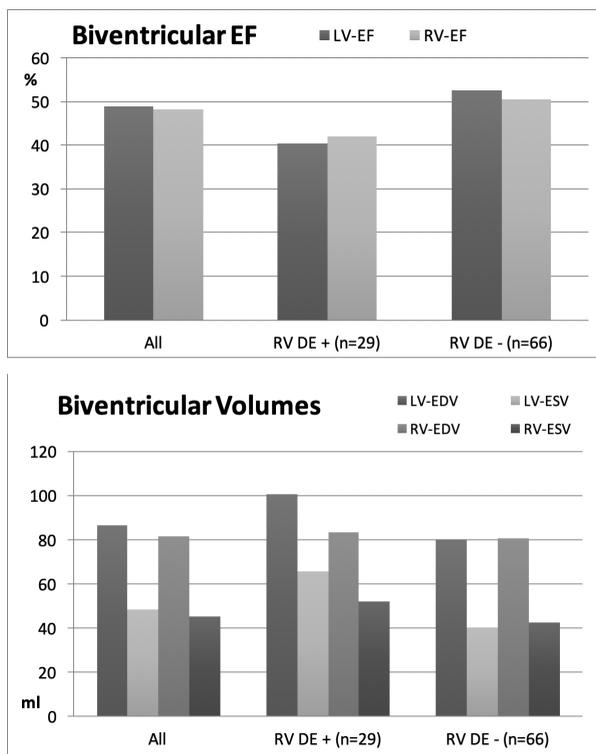


Figure 4. Biventricular Ejection Fraction and Volumes. The figure shows biventricular ejection fraction (Upper Panel) and volumes (Lower Panel) in the two subgroups (Patients with RV delayed enhancement and patients without RV involvement).
Abbreviations: RV = Right Ventricle; EF = Ejection Fraction; EDV = End-Diastolic Volume; ESV = End-Systolic Volume.

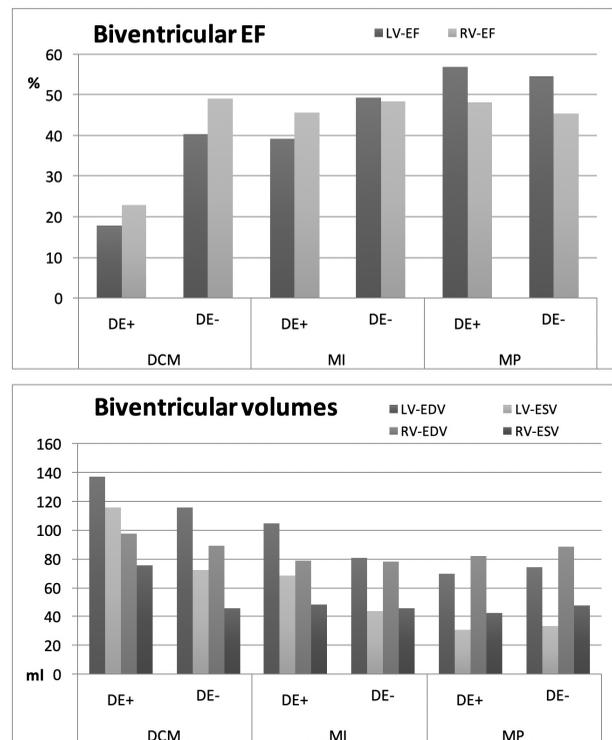


Figure 5. Biventricular Ejection Fraction and Volumes in subgroups. The figure shows biventricular EF and Volumes in patients with dilated cardiomyopathy, myocardial infarction and myocarditis/pericarditis. The figure shows that patients with a dilated cardiomyopathy or a myocardial infarction and a positive RV DE have a worse cardiac function with a lower ejection fraction (Upper Panel) and higher biventricular volumes if compared with RV DE- subgroup (Lower Panel).
Abbreviations: RV = Right Ventricle; LV = Left Ventricle; DCM = dilated cardiomyopathy; MI = myocardial infarction; MP = myocarditis/pericarditis; EF = Ejection Fraction; EDV = End-Diastolic Volume; ESV = End-Systolic Volume.

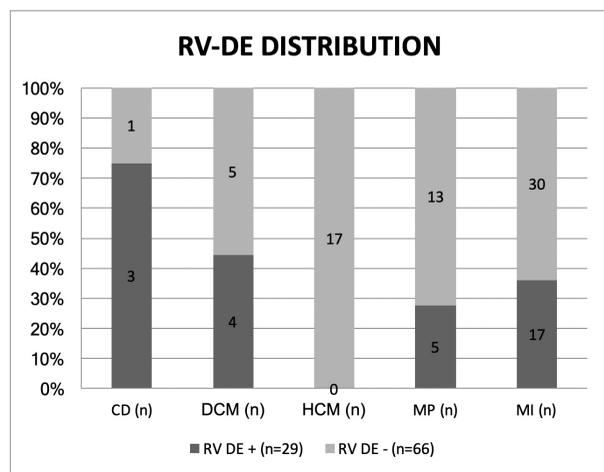


Figure 6. Right Ventricular Delayed Enhancement in subgroups. The figure shows the distribution of Right Ventricle Delayed Enhancement in the different subgroups, it predominantly concerns patients with ischemic heart diseases. No patients with hypertrophic cardiomyopathy had RV DE.

Abbreviations: RV = Right Ventricle; CD = congenital disease; DCM = dilated cardiomyopathy; HCM: hypertrophic cardiomyopathy; MP = myocarditis/pericarditis MI = myocardial infarction.

Discussion

In this study we evaluated the prevalence and features of concomitant involvement of the RV in patients with LV-DE using CMR. Myocardial scar (i.e. fibrosis) at CMR is visualized as an area of “delay enhancement”. The presence of DE is associated with several cardiac diseases and it is due to the expansion of extracellular space in comparison to normal myocardium.

Fibrosis contributes to right ventricle functionality impairment and pulmonary hypertension development (13); so its identification is crucial in the prevention of complications such as right ventricle overload and pulmonary hypertension.

The localization together with the extension and distribution helps in differential diagnosis (14). In myocarditis, DE is typically due to necrosis in the early phase and scar development in the late phase (14). In HCM patients, DE has been detected in a range of patients between 33% and 84%, generally with a patchy mid-wall pattern in hypertrophic points and at the anterior and posterior RV insertion points in the ventricular septum adjacent to the attachment to the RV free wall (15, 16).

In HCM patients, RV fibrosis of the free wall, is a possible cause of diastolic dysfunction and arrhythmias, so RV detailed evaluation should be included in HCM patients (17).

In our population, no right ventricular involvement in HCM was found probably due to the small sample examined.

LV-DE is easier to detect due to the thicker ventricular wall and most of literature is based on the study of LV involvement (18). LV can be analysed both with CMR and computed tomography (CT) (19). In particular DE and cardiac function can be both evaluated also with computed tomography as demonstrated in the literature (20-24).

In CMR in case of RV-DE suspicion, it is necessary to carefully adjust the inversion time to maximize the contrast between remote and fibrotic myocardium.

In this study, we aimed to demonstrate that RV involvement is frequent, underestimated and common to different diseases and, for this reason, RV evaluation should be introduced in clinical and daily practice. Furthermore, right ventricular fibrosis could be visualised in the absence of ECG or echocardiographic signs; indeed, in our population, only 59% of the RV-DE+ patients showed at the same time ECG abnormalities and only 55% had any echocardiographic suspicion. Jensen et al. (9) demonstrated that RV involvement in patients with acute LV MI is an independent prognostic indicator for MACE and that CMR is superior to ECG and echocardiography for the detection of RV involvement. Patient prognosis was not evaluated at this stage even though RV-DE+ patients had a worse biventricular function with a worse EF and dilated chambers.

Our study has some limitations: first of all, it is a retrospective study without prognostic data, the aim was to assess the diagnostic performance and the values of functional parameters; for this reason, prognostic data will be collected for this population in the future. The second limitation is the relatively small population for subgroup analysis. Nevertheless, the patterns detected highlight the important functional impact of RV involvement on LV and RV functional parameter. Finally, the incidence and importance of RV-DE is significantly affected (and eventually biased) by the specific heterogeneity of the study population.

In conclusion, RV-DE in patients with LV primary involvement is not negligible and can be easily evaluated by CMR DE also in absence of ECG or echocardiographic anomalies. It is more often associated with biventricular functional alterations and predominantly concerns patients with ischemic heart diseases.

Conflicts of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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