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Cardiac magnetic resonance in patients with mitral valve prolapse: Focus on late gadolinium enhancement and T1 mapping

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Abstract

Objectives To evaluate the incidence of late-gadolinium-enhancement (LGE) in mitral valve prolapse (MVP) (in the absence of other heart/valvular diseases), and its association with the degree of mitral regurgitation (MR) and/or with complex ventricular arrhythmia (ComVA), and to analyse the role of T1 mapping in the evaluation of MVP patients.

Methods We included all consecutive patients with MVP who underwent during 2015–2016 a comprehensive cardiac magnetic resonance (CMR) examination at 1.5 T. We evaluated the association of LGE with the MR fraction and the presence of ComVA. We compared myocardial T1-native and post-contrast times and extracellular volume (ECV)-values between MVP patients, both with and without LGE, and the control group.

Results Thirty-four patients with MVP were selected (56 ± 14 years old, 59% male). All patients had MR; LGE and ComVA were present in 15 (44%) and 11 (34%) patients, respectively. Significant associations of LGE with both MR severity and ComVA were not found (p=0.72 and 0.79, respectively). T1 mapping confirmed the presence of LGE in all cases. In one patient a thin signal alteration resulted in more evident T1 mapping than LGE. Patients with MVP had higher native T1-values, lower post-contrast T1-values and increased ECV-values compared with controls (p=0.01, 0.01 and 0.00, respectively).

Conclusion Focal fibrosis with LGE was found in about half the MVP patients and it was independent of the degree of the valve dysfunction and the presence of ComVA. T1 mapping allows diffuse myocardial wall alterations to be identified, but no significant associations between the MR severity and ComVA and T1/ECV values were found.

Key Points

- *MVP is a common valvulopathy affecting 2–3% of the general population.*
- *MVP has been associated with an increased risk of arrhythmic complications and sudden cardiac death.*
- *CMR is a non-invasive imaging method that provides a precise and more accurate assessment of patients with MVP.*

Keywords Cine magnetic resonance imaging · Prolapsed mitral valve · Gadolinium · T1 mapping

Abbreviations

2C	2-chamber
3C	3-chamber
4C	4-chamber
AHA	American Heart Association
CMR	Cardiac magnetic resonance
ComVA	Complex ventricular arrhythmias
ECV	Extracellular volume
LGE	Late gadolinium enhancement
LV	Left ventricular
MOLLI	Modified Look-Locker inversion
MR	Mitral regurgitation
MVP	Mitral valve prolapse
PACS	Picture Archiving and Communication System
PSIR	Phase-sensitive inversion recovery
RV	Right ventricular
SA	Short-axis

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SCD Sudden cardiac death
SSFP Steady-state free processing
SV Stroke volume

Introduction

Mitral valve prolapse (MVP) is a common valvulopathy that affects 2–3% of the general population [1].

Although MVP is generally regarded as a benign condition, its outcome is widely heterogeneous, and complications can be severe [2]. MVP is defined as > 2 mm displacement of the mitral leaflets into the left atrium when viewed in the left ventricular (LV) outflow tract orientation [3]. Echocardiography remains the most relevant diagnostic modality for MVP. The 2014 guidelines of the American Heart Association (AHA) recommend cardiac magnetic resonance (CMR) when the quality of ultrasound images does not allow for an appropriate evaluation [4]. In recent years, there has been an increase in the use of CMR to assess valvular heart disease, due not only to the growing prevalence of this disease [5], but also to technical CMR improvements/availability and the introduction of new treatment options [6]. CMR allows for a precise evaluation of ventricular volumes, systolic function, valvular morphology and the degree of mitral regurgitation (MR), all of which may improve patient assessment and facilitate improved pre-procedural patient selection. Furthermore, CMR can highlight areas of myocardial injury/fibrosis with late gadolinium enhancement (LGE) [3]. More recently, T1 mapping has proved to be a promising CMR technique in the setting of diffuse fibrosis and extra-cellular matrix evaluation for ischaemic or non-ischaemic cardiomyopathies [7–11]. MVP can be associated with MR in relation to the grade of valve apparatus dysfunction. It is accepted that CMR is more accurate than echocardiography in assessing the severity of MR [12]. MVP patients with left ventricular dysfunction resulting from severe MR were considered as a subgroup at high risk of sudden cardiac death (SCD) [2] and were recommended to undergo surgery, even in the absence of symptoms [13]. However, life-threatening ventricular arrhythmias and SCD can occur even in MVP patients with absent or mild MR [14–16]. In the general population in the Framingham study, the prevalence of MVP among the SCD victims reported by Freed and colleagues stands at 2.4% [17].

However, the relationship between SCD and MVP is still a challenging issue. Arrhythmias appear to play an important role, while the structural substrate for electric instability remains uncertain [17]. In this retrospective study, our aim had been to analyse the incidence of LGE abnormalities in patients with MVP (no other heart pathologies) and its association with the degree of mitral MR and/or with complex ventricular arrhythmia (ComVA). We also evaluated T1-mapping sequences compared to standard CMR sequences. Understanding whether the presence of LGE and T1-mapping alterations are relevant for this group of patients might help to optimise the indications for CMR and assess its role in arrhythmic risk stratification.

Materials and methods

Patient population

From a search on our Picture Archiving and Communication System (PACS) ('mitral valve' and 'cardiac magnetic resonance'), we selected all patients with MVP who had undergone a complete CMR between December 2015 and December 2016. By studying medical records, we excluded MVP patients with other heart conditions (including other valvular problems). All the patients had provided informed consent in writing for the CMR examination with IV administration of CA (including an eligibility and exclusion form for the CMR examination). The patients' records were anonymised and de-identified prior to analysis.

We compared myocardial T1 times between MVP patients and a control group. We chose as controls the patients who had performed the CMR as part of sport medical tests. All of these subjects were asymptomatic without any sign of pathology at CMR.

Analysis of arrhythmias

We analysed the presence of arrhythmias in our study population. Patients with MPV afferent to our hospital were evaluated in the same cardiac division, with the same equipment, on a 12-lead 48- to 72-h ECG Holter monitoring system (Mortara H12) requested because of the presence of arrhythmic symptoms or 12-lead ECG changes. Holter or event monitor arrhythmia data were available within 12 months of CMR. ComVA was defined as grade III or higher by the Lown and Wolf classification [18]. The absence of ComVA was determined by a negative Holter or event monitor, or by the absence of symptoms (palpitations or skipped beats) and no ambulatory ECG record of ventricular arrhythmias during the follow-up within 12 months preceding the CMR.

CMR protocol

CMR images were acquired using a 1.5 T MR scanner Magnetom Aera (Siemens Medical Solutions, Erlangen, Germany). ECG-gated cine steady-state free processing (SSFP) images were acquired in the 2-chamber (2C), 3-chamber (3C) and 4-chamber (4C) horizontal long-axis views, and a short-axis (SA) stack covering the entire LV (6-mm slices without a gap, 10–15 slices). The 2C and 4C views were perpendicular to the short axis of the left ventricle, obtained

with a single breath-hold and with the ECG trigger (capture cycle gating; see the sequence parameters in Table 1). The LV outflow tract long-axis view was obtained by prescribing an image plane perpendicular to the mitral annular major axis centred at the aortic outflow track. Free-breathing, ECG-triggered phase-contrast velocity sequences for ascending aortic and pulmonary flow were acquired.

Phase-contrast imaging with velocity-encoded imaging was used to estimate the aortic forward flow and calculate the regurgitation fraction. Ten minutes after the administration of a 0.1 mmol/kg gadobutrol injection (Gadovist, Bayer HealthCare), infused at 1 ml/s, followed by 20 ml saline with an automated injector (Medrad Spectris Solaris injector and Veris monitoring system, Bayer HealthCare Pharmaceuticals, Berlin, Germany), ECG-gated breath-hold 2D PSIR LGE-CMR was performed in the 2C, 3C and 4C turbo flash phase-sensitive inversion recovery (PSIR)-LGE and short-axis orientations, corresponding to the SSFP cine slices TRUFI PSIR-LGE. For T1 mapping, we used ECG-triggered acquisitions modified by Look-Locker inversion recovery (MOLLI), using the scheme 3(3)3(3)5. Post-contrast MOLLIs were performed for 15–20 min after the gadolinium bolus, using the scheme 4(1)3(1)2. CMR data were analysed using a dedicated workstation (IntelSpace, Philips Medical Systems, Best, The Netherlands).

CMR image analysis

Two independent radiologists (SP and LC, with 15 and 5 years of experience, respectively, in CMR) retrospectively quantified the MR fraction. They visually assessed the presence of myocardial LGE, and qualitatively and quantitatively evaluated T1-mapping sequences before arriving at a consensus.

Mitral regurgitation fraction

By tracing the end-diastolic and end-systolic LV and RV endocardial contours in each short-axis slice, and by applying a summation of the slices method we measured LV and RV volumes, and LV mass. The papillary muscles were considered a part of the ventricular volumes. The LV ejection fraction was calculated as: 100 × (LV end-diastolic volume−LV end-systolic volume)/LV end-diastolic volume. The total LV and RV stroke volumes (SVs) were obtained by subtracting the LV and RV end-systolic volume from the LV and RV end-diastolic volume, respectively. The aortic forward flow volume was obtained from 2–3 cm above the aortic valve in an orthogonal orientation to the aortic root. Correction for baseline flow offsets was performed using a dedicated phantom. Flow measurements from three acquisitions were averaged.

First, we quantified isolated mitral regurgitation using the 'volumetric' indirect method as follows [19]: mitral regurgitant volume = LVSV– RVSV.

Second, to confirm the obtained value, the mitral regurgitant volume was calculated according to the 'standard' indirect method, by subtracting the total LVSV volume from the aortic forward flow volume (LVSV – aortic forward flow) [19].

Finally, the mitral regurgitant volume was also quantified as the mitral regurgitant fraction as follows: mitral regurgitant fraction % = (regurgitant volume × 100) /LVSV.

Based on the existing literature, we identified different groups [20]:

Mild mitral regurgitant fraction < 20%
Moderate mitral regurgitant fraction = 20–40%
Severe mitral regurgitant fraction > 40%

Late gadolinium enhancement

The presence of myocardial LGE was determined when part of the myocardial tissue present in the SSFP images was replaced by high signal intensity in the LGE images. LGE was visually estimated based on the AHA 17-segment model [21]. Readers assessed the presence and the site of LGE. LGE

Table 1 Scan parameter of a cardiac magnetic resonance (CMR) protocol

Parameter	Trufi cine (2C, 3C, 4C)	SA Trufi cine	LGE Turbo FLASH PSIR (2C, 3C, 4C)	SA LGE Trufi PSIR	PC	T1 MOLLI native 3(3) 3(3) 5 MOCHO	T1 MOLLI post-contrast 4(1) 3(1) 2 MOCHO
FOV	360	360	340	340	370	360	360
TR (ms)	31	31	713	713	40	311.46	311.46
TE (ms)	1.3	1.3	3.21	1.12	2.9	1.12	1.12
Flip angle (°)	60	60	25	40		35	35
Slice thickness (mm)	8	6	8	8	6	8	8
IT (ms)			300–380	300–380		192	272

Localiser sequences: TRUFI axial, sagittal and coronal. For phase contrast images the velocity encoding VENC was optimised for each patient

TRUFI true fast imaging with steady-state free precession, *PSIR* phase sensitive inversion recovery, *LGE* late gadolinium enhancement, *PC* phase contrast, *MOLLI* Modified Look-Locker-Inversion recovery, *TR* time of repetition, *TE* time to echo, *IT* inversion time, *2C* 2-chamber, *3C* 3-chamber, *4C* 4-chamber, *SA* short axis

patterns have been described depending on myocardial wall involvement as subendocardial, mid-wall and epicardial. The association of LGE with the degree of the MR fraction and the ComVA was evaluated.

T1 mapping

T1 mapping before (native) and after gadolinium administration was qualitatively evaluated by radiologists and compared with LGE images. The T1 relaxation time value was calculated within a region of interest (ROI) (approximately 10 pixels) in the septum, in the inferolateral wall at the basal level, and in focal lesions if present. The synthetic extracellular volume (ECV) was calculated without haematocrit sampling, as recently proposed and validated by Treibel et al, in the following manner: Synthetic Hct MOLLI=(866.0×[1/T1 blood])-0.1232 [22]; ECV=[(ΔR1 myocardium/(ΔR1 blood pool)×(1-Hct MOLLI)], where ΔR1=1/T1 post-contrast-1/T1 pre-contrast. [23]. ECV within the septum and at the inferolateral basal wall was averaged to yield a global ECV measurement. We compared myocardial T1 native and post-contrast times and mean ECV values between MVP patients and the control group. Finally, we compared the same parameters in the MVP population between LGE-positive and LGE-negative patients.

Statistics

GraphPad Prism v7.0 (GraphPad Software Inc., La Jolla, CA, USA) was used to perform all statistical analyses. Clinical characteristics of the participants were presented as mean ± SD. Normal distribution was assessed using the Shapiro Wilk test. Comparisons between groups were made using the $\chi 2$ or Fisher's exact test for categorical data. A p value of <0.05 was considered significant. The interobserver agreement for MR fraction quantification was assessed with Cohen's kappa ($k \leq 0.39$, poor agreement; $k = 0.40$–0.59, fair agreement; $k = 0.60$–0.74, good agreement; $k \geq 0.75$, excellent agreement).

Results

Fifty-two consecutive patients with diagnosed MVP who had undergone a complete CMR examination from December 2015 to December 2016 were included in the study. After an examination of medical records, 16 patients with MVP were excluded from the study as they had other valvular diseases, coronary artery disease, hypertension or other intrinsic cardiomyopathies. Out of 36 MVP patients without other heart conditions, two were excluded for poor CMR image quality due to arrhythmia. Finally, a total of 34 patients (20 male and 14 female patients, mean age 56 ± 14 years) were included in our study. The baseline clinical and CMR findings of the 34 MVP patients are summarised in Table 2. In the control group (15 male and 15 female patients) the mean age was 40 ± 5 years.

Arrhythmias

The study population had 11/34 (32%) patients with ComVA and 23/34 (68%) patients without ComVA. In particular, one of the patients with ComVA had ventricular tachycardia non-sustained, seven patients had multiform ventricular premature beats and three patients had repetitive ventricular premature beats (couplets).

Mitral regurgitation

The concordance rate for MR fraction quantification between the two readers was excellent (Cohen's kappa >0.85). MR was observed in all the MVP patients who had undergone CMR: 12 patients (35%) with mild regurgitant fraction, 15 patients (44%) with moderate regurgitant fraction and seven patients (20%) with severe regurgitant fraction.

LGE

The presence of LGE was found in 15 MVP patients (44%). Eight patients had mid-wall myocardial LGE of the basal inferolateral wall (Fig. 1), with one of them showing evidence of papillary muscle fibrosis (Fig. 2). Five subjects showed the presence of LGE on the valve and at the level of mitral annulus (lateral), with one showing LGE in the papillary muscle. Furthermore, two patients had LGE in the basal interventricular septum (Fig. 3). LGE was detected in 1.5 segments on average. MVP patients with LGE did not show any significant difference in the severity of mitral regurgitation (33% mild, 40% moderate and 27% severe). The proportion of patients with LGE who had severe MR (27%, 4/15) was not significantly different in the group of MVP patients without LGE (3/19, 16%) (p=0.72).

In terms of arrhythmias, no statistically significant differences were found between MVP patients with LGE and those without LGE. In particular, ComVA was found in 5/15 (33%) MVP patients with LGE and in 6/19 (31%) MVP patients without LGE (p=0.79).

T1 mapping

T1 mapping confirmed the presence of LGE in all cases (Figs. 3 and 4). In particular, in one patient the thin signal alteration resulted in being more evident in T1 mapping than in LGE images, where the readers only suspected the lesion. Patients with MVP had significantly higher native and lower after-contrast T1-values than controls (all $p<0.05$) (Table 3). No statistically significant differences were found between the native T1 of the focal lesion in MVP patients with LGE and the native

Table 2 Clinical and cardiac magnetic resonance (CMR) characteristics

	Overall MVP (n=34)	MVP with LGE (n=15)	MVP without LGE (n= 19)	*p*-value
Age (y)	56 ± 14	56 ± 12	55 ± 15	0.83
Male, n (%)	20 (59%)	9 (60%)	11 (58%)	0.82
Female, n (%)	14 (41%)	6 (40%)	8 (42%)	0.82
Diabetes, n (%)	0 (0%)	0 (0%)	0 (0%)	N/A
Hypertension, n (%)	0 (0%)	0 (0%)	0 (0%)	N/A
Smoking history, n (%)	14 (41%)	7 (46%)	7 (37%)	0.82
Hyperlipidaemia, n (%)	7 (20%)	3 (20%)	4 (21%)	0.72
NYHA class I, n (%)	27 (79%)	11 (73%)	16 (84%)	0.72
NYHA class II, n (%)	7 (20%)	4 (27%)	3 (16%)	0.72
NYHA class III, n (%)	0 (0%)	0 (0%)	0 (0%)	N/A
NYHA class IV, n (%)	0 (0%)	0 (0%)	0 (0%)	N/A
Palpitations, n (%)	14 (41%)	6 (40%)	8 (42%)	0.82
Syncope, n (%)	2 (5%)	0 (0%)	2 (10%)	0.63
Family history of CAD, n (%)	5 (14%)	2 (13%)	3 (16%)	0.77
Family history of SCD, n (%)	0 (0%)	0 (0%)	0 (0%)	N/A
LV EDV, ml	168 ± 43	174 ± 37	163 ± 48	0.46
LV EF, %	61 ± 5	62 ± 3	61 ± 7	0.60
LV mass, g/m^2	124 ± 46	138 ± 43	114 ± 46	0.13
MR mild, n (%)	12 (35%)	5 (33%)	7 (37%)	0.88
MR moderate, n (%)	15 (44%)	6 (40%)	9 (47%)	0.93
MR severe, n (%)	7 (20%)	4 (27%)	3 (16%)	0.72

Categorical variables are presented as number of patients (%); continuous values are expressed as mean ± SD

MVP mitral valve prolapse, *LGE* late gadolinium enhancement, *LV* left ventricular, *EDV* end-diastolic volume, *EF* ejection fraction, *MR* mitral regurgitation, *N/A* not applicable, *NYHA* New York Heart Association functional class, *CAD* coronary artery disease, *SCD* sudden cardiac death

T1 at the inferolateral wall of MVP patients without LGE (p=0.52) (Table 4). As shown in Table 3, MVP patients had significantly higher median ECV values than the control group (p<0.05), whereas no statistically significant differences were found in terms of ECV values between MVP patients with LGE and those without LGE (p=0.39) (Table 4). Furthermore, no significant association between the MR severity and ComVA and T1/ECV values was found.

Discussion

In our series, the presence of LGE in patients with MVP and without any other heart problems was found in almost half of the cases. LGE is independent of the degree of valve dysfunction. No significant associations were found between LGE and ComVA. T1 mapping significantly confirmed LGE, and it was more sensitive in identifying alterations in one patient.

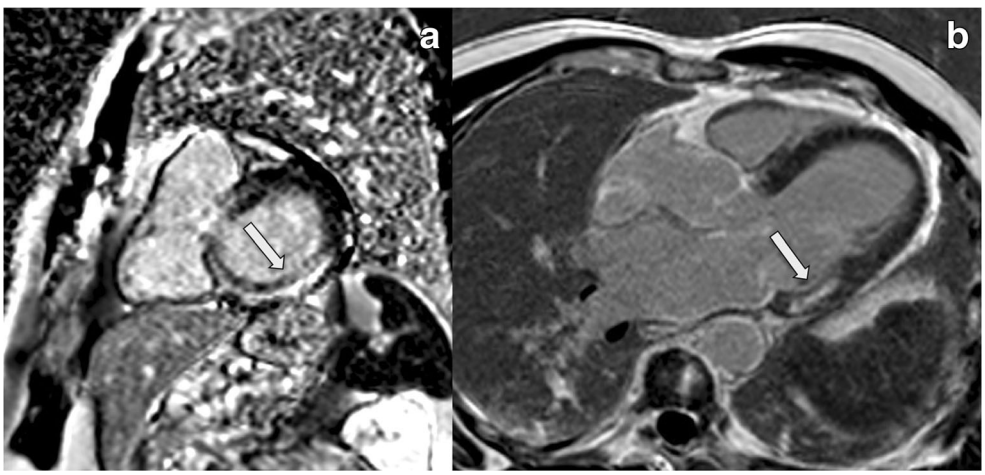

Fig. 1 The late gadolinium enhancement (LGE) images show a bright alteration in the infero-lateral wall (arrows) on short axis (**a**) and 3-chamber (**b**) images

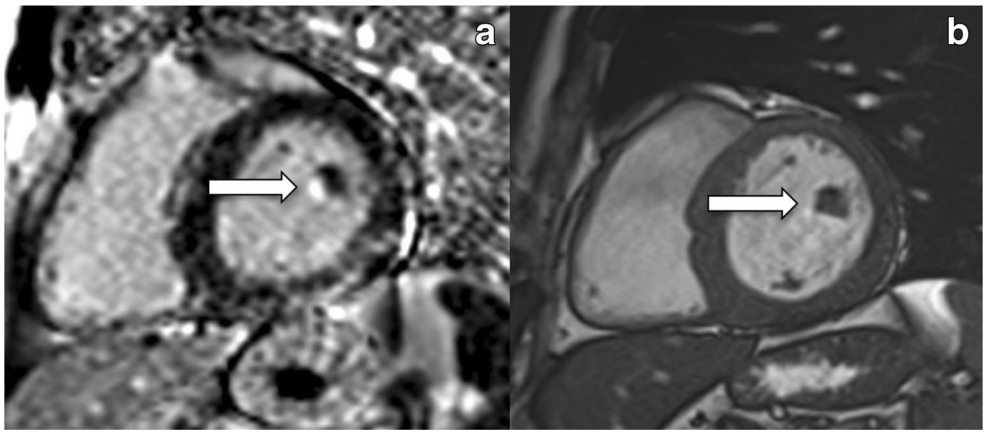

Fig. 2 (**a**) Late gadolinium enhancement (LGE): focal type of papillary muscle fibrosis (arrow). (**b**) TRUFI cine image at the same level, papillary muscle (arrow)

Patients with MVP had higher T1 values in native maps and increased ECV values than those in the control group. We did not observe statistically significant differences between the native T1 time at the infero-lateral wall of patients without LGE and the native T1 of the focal lesion of patients with LGE.

At a time when interventions for mitral valve disease are both improving and recommended early in the disease course (a 2008 focused update incorporated 2006 guidelines for the management of patients with valvular heart disease into the American College of Cardiology/AHA), it becomes important to assess MVP patients with a precise and accurate modality such as CMR, which is essential in determining the natural history of degenerative mitral valve disease [15].

The role of the CMR in patients with MPV has not been completely elucidated so far. Until recently, the investigation of patients with valvular disease included only the cine and the phase-contrast sequences. Similar to our study, published studies to date have included a limited number of patients. Nonetheless, new additional data may help to better define the role of LGE and T1 mapping. In our study, LGE was present equally in those patients with arrhythmias and in those without. T1 mapping seemed extremely useful for confirming LGE and to highlight the presence of a diffuse alteration.

Previous studies suggested that LGE could be present in up to 30% of patients with moderate to severe MR, and that left ventricular remodelling seems to be associated with the presence of LGE in primary MR [24]. Recently, Marra et al [25] and Basso et al [2] have demonstrated that the evidence of the substrate of electric instability in MVP consists of myocardial scarring that targets the papillary muscles and the infero-basal LV free wall, in keeping with the site of origin of ventricular arrhythmias. An autopsy series done by Sheppard et al confirmed the findings of Basso et al, suggesting that in the subgroup of patients with MVP with increased-risk clinical indications and mainly ComVA, LGE can play a crucial role in the risk stratification assessment of these patients [26]. A recent review of the literature over the last 15 years highlighted the controversy concerning the association of MVP with ventricular arrhythmias and SCD, emphasising the need for further experimental investigation to define the role of imaging and genetic evaluation in risk stratification for SCD in MVP patients [27].

CMR is a well-established, non-invasive imaging method that provides reproducible quantitative data on cardiac anatomy and function. It is a flexible modality with unlimited imaging planes available. It is the gold-standard measurement for LV volumes and function [20]. Cine CMR methods allow for

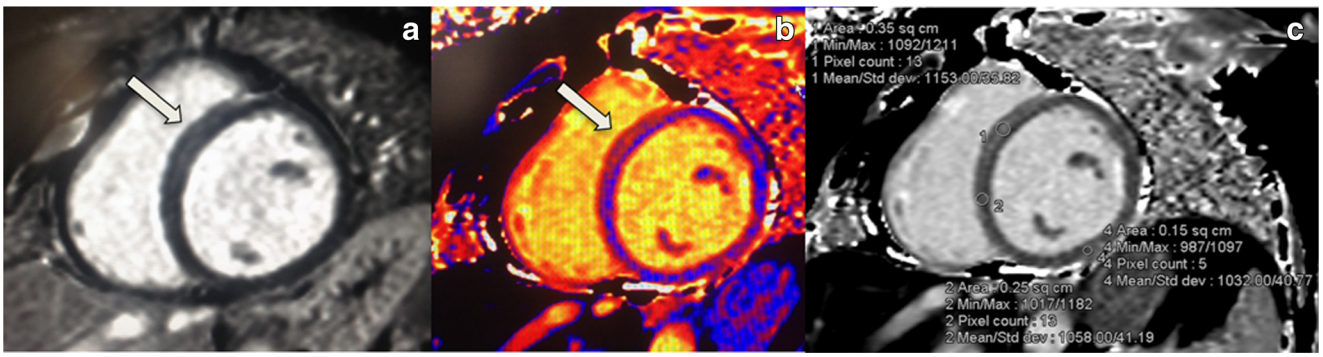

Fig. 3 Short axis late gadolinium enhancement (LGE) (**a**) shows a slight area of hyper-enhancement in the mid wall anterior septum (arrow), confirmed by a colour T1 native map (**b**) and T1 map values (**c**) at the level of the anterior septum (1150 ms) vs. the inferior septum and lateral wall (1050 ms and 1030 ms, respectively)

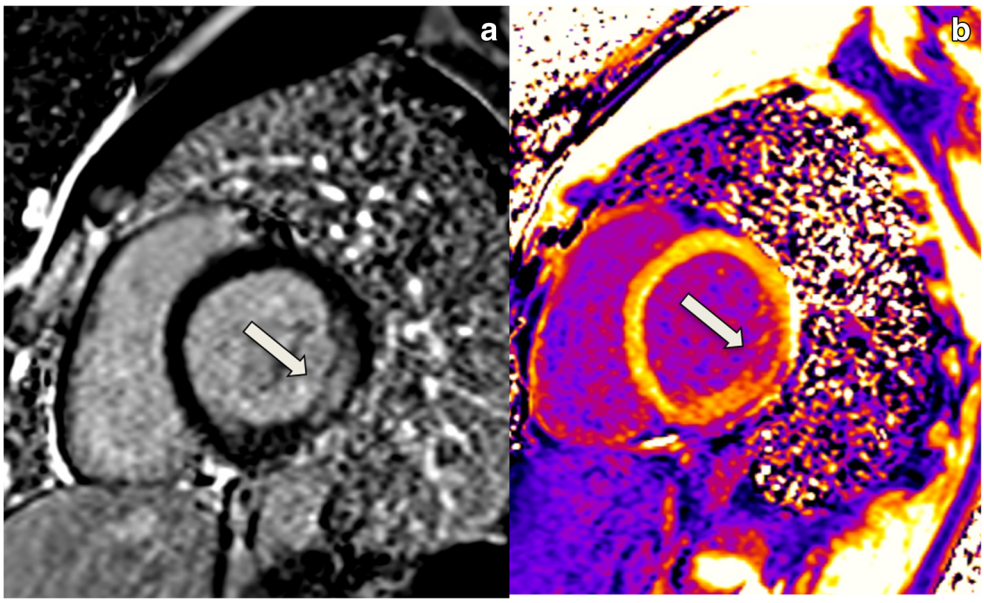

Fig. 4 (**a**) Short axis late gadolinium enhancement (LGE) shows a mid-wall area of hyper-enhancement at the infero-posterior wall (arrow). (**b**) The alteration is confirmed by a T1 post-contrast coloured map

the characterisation of valve morphology. Additionally, phase-contrast CMR can easily quantify aortic and pulmonary flow velocities and volumes. These data can be combined with LV/RV volumetric data to determine the atrioventricular regurgitant volume and fraction [19, 28, 29]. Moreover, because CMR does not rely on the direct assessment of the regurgitant jet, quantifying eccentric or multiple regurgitant jets is not problematic. As with echocardiography, this could be important for clinical decision-making and is an additional value of CMR imaging [29]. In our study, we used two indirect methods to assess MR and MR fraction, as phase-contrast velocity sequences at the mitral valve annulus ('direct method') were less validated [30], due to the highly mobile nature of the valve and the often-eccentric jets of MR. The agreement between the two observers for the MR fraction evaluation was very good (Cohen's kappa > 0.85).

In our series we found LGE alterations in about half the patients. Therefore, the incidence of LGE in patients with MVP is significant and CMR could be an accurate modality to better assess MVP patients thanks to its ability to characterise myocardial tissue changes. In line with recent studies [25], we demonstrated that CMR could detect focal myocardial fibrosis typically involving the papillary muscle or basal infero-lateral wall as the hyper-enhancement areas on LGE. We did not find significant differences in the severity of MR among the MVP patients with LGE. Focal fibrosis was present even with mild MR. These data support the theory that LV fibrosis is the consequence of MVP as a result of a systolic mechanical stretch of the myocardium, which is closely linked to the valve (papillary muscles and infero-basal wall) by the prolapsing leaflets and elongated chordae [25]. Considering that, all patients with MVP, regardless of the degree of valve dysfunction, should undergo CMR in order to evaluate the presence of myocardial injury/fibrosis on LGE, which is considered as a structural substrate of arrhythmias by Marra et al [25]. Nevertheless, we did not find in our patients a significant association between LGE and ComVA.

With regard to T1 mapping, the qualitative analysis of pre- and post-contrast T1 maps was helpful in confirming the LGE areas, which in one case was easier to identify on the map than the LGE sequences. These maps, both before and after contrast administration, even in the coloured version, helped us to recognise the presence of an alteration (different colour, higher/lower T1 value) with increasing confidence. In our

Table 3 MVP patient's and control group's segmental MOLLI T1 relaxation times and MOLLI T1-derived ECV

	MVP patients (n=34)		Control group (n=30)	*p*-value
T1 MOLLI Native (ms)	Basal inferolateral	1110.5 ± 55	1007.5 ± 51	0.0001
	Basal septum	1023.5 ± 92	983 ± 41	0.0122
T1 MOLLI post-contrast (ms)	Basal inferolateral	443.5 ± 70	514.5 ± 85	0.0002
	Basal septum	456.5 ± 17	489.5 ± 78	0.0180
MOLLI ECV (%)	30.5 ± 2		23.5 ± 0.7	0.0000

Numbers are given as mean ± SD. Post-contrast T1 values were obtained 15–20 min after contrast administration

MOLLI Modified Look-Locker Inversion Recovery, *MVP* mitral valve prolapse, *ECV* extracellular volume fraction, *MVP* mitral valve prolapse, *LGE* late gadolinium enhancement

Table 4 Segmental MOLLI T1 relaxation times and MOLLI T1-derived ECV of the MVP patients, with and without LGE

		MVP patients with LGE (n=15)	MVP patients without LGE (n=19)	*p*-value
T1 MOLLI native (ms)	Basal inferolateral	1047 ± 34	1122.5 ± 39	0.0000
	Basal septum	1014.5 ± 80	1070 ± 26	0.0076
	Focal lesion	1135.5 ± 77		0.5262 vs. basal inferolateral of MVP without LGE 0.0015 vs. basal septum of MVP without LGE
T1 MOLLI post-contrast (ms)	Basal inferolateral	430 ± 18	460 ± 22	0.0002
	Basal septum	455.5 ± 19	465.5 ± 30	0.2696
	Focal lesion	365 ± 19		0.0000 vs. basal inferolateral of MVP without LGE and vs. basal septum of MVP without LGE
MOLLI ECV (%)		32 ± 3	31 ± 5	0.3892

Numbers are given as mean ± SD. Post-contrast T1 values were obtained 10 min after contrast administration

MOLLI Modified Look-Locker Inversion Recovery, *MVP* mitral valve prolapse, *LGE* late gadolinium enhancement

opinion, this is essential not only when the alteration is slight in LGE but also with no focal alterations. To the best of our knowledge, only two original papers analysed myocardial T1 time in patients with MVP to assess the presence of diffuse myocardial fibrosis. In these studies, Bui et al found that patients with MVP had significantly shorter post-contrast T1 times, suggesting diffuse myocardial fibrosis, when compared with controls. Furthermore, patients with MVP with ComVA showed significantly shorter post-contrast T1 times when compared with patients with MVP without ComVA [16]. Edwards et al demonstrated higher ECV-values in patients with moderate/severe MR than controls, but with wider overlap at the upper end of the normal range [31]. Additionally, we found that patients with MVP, including those with mild MR, had higher T1 values in native T1 maps and an increased ECV compared with the control group. This strengthens the assumption that there is a wall alteration, probably due to fibrosis (even non-focal), where extracellular space is increased. Furthermore, we found no statistically significant differences in terms of ECV values between MVP patients with LGE and those without LGE. We also observed that native T1 time at the infero-lateral wall of patients without LGE was not statistically significantly different from native T1 of the focal lesion of patients with LGE. Therefore, patients with MVP had myocardial alterations even if no area of hyper-enhancement was found. The T1 mapping identification and quantification of this alteration, even in the absence of LGE, could be a further tool for a better evaluation of these patients.

The present study has some limitations. First, this was a retrospective observational study despite the MRI protocol remaining the same. Second, the patient cohort was small due to the short period of analysis, because T1-mapping sequences have only recently been included in our CMR protocol. Finally, the small number of MVP patients with ComVA could explain the poor association between ComVA and LGE in our patient cohort. Accordingly, the small number of arrhythmic patients in our study population would have invalidated the statistical power of the relationship between T1 mapping alterations and ComVA. Despite these restrictions, our study emphasises the high frequency of LGE and T1 mapping alterations in MVP patients, regardless of the degree of valve dysfunction and the presence of ComVA.

In conclusion, in our series, CMR detected myocardial fibrosis in about half the MVP patients, without an association either between LGE and the degree of valve dysfunction or between LGE and ComVA. Patients with MVP had higher T1 values in native maps and increased ECV than their control group counterparts, even without LGE. While the relationship between fibrosis and arrhythmias has received increasing attention, T1 mapping is a new promising application that allows identification of a myocardial wall alteration, even non-focal in nature. Prospective studies should consider a larger patient cohort to establish if T1-mapping alterations are a marker of arrhythmic risk in MVP patients, regardless of the degree of MR.

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Compliance with ethical standards

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Ethical approval Institutional Review Board approval was obtained.

Methodology
- Retrospective
- Observational
- Performed at one institution

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