Late gadolinium enhanced-cardiac magnetic resonance (LGE-CMR) quantification of myocardial damage as a predictor of arrhythmic events

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Purpose

Patients with hypertrophic cardiomyopathy (HCM) are predisposed to ventricular tachyarrhythmias (VT) that seem to be the primary cause of Sudden Cardiac Death (SCD) [1].

Irreversible myocardial replacement scarring is recognized as the anatomical and electrophysiological substrate for the occurrence of VT and SCD in patients with HCM [2].

Late gadolinium-enhanced (LGE) cardiovascular magnetic resonance (CMR) is a new non-invasive technique that allows visualization and quantification of myocardial scarring in HCM patients [3].

Implantable cardioverter-defibrillator (ICD) correct potentially lethal arrhythmias in HCM [4] but the selection of patients for implantation is presently performed on the bases of different techniques (24 hours ECG-Holter monitoring, history of SCD) all with low predictive accuracy [5].

The aim of the present study is to investigate the prognostic value of LGE-CMR in predicting the occurrence of Sustained Ventricular Tachyarrhythmias (SVT) and Implantable Cardioverter Defibrillator Shock (ICDS) on the bases of LGE extension in HCM patients.
Methods and Materials

Study population

It’s a non-randomized single centre study with prospective evaluation, performed between August 2005 and August 2011 at the Institute of Radiology, University Hospital of Modena, Italy. Local ethic committee approved the study.

The study population is composed by 62 patients (mean age: 55.6±16.0; 67.7% males) with the diagnosis of HCM based on using history, clinical examination, echocardiography, coronary angiography and 24 h ECG Holter-monitoring (Fig. 1).

Exclusion criteria: clinical history of atherosclerotic coronary artery disease, systemic or specific cardiac cause of hypertrophy, general MR imaging contraindications.

Written Informed consent was obtained by all subjects.

LGE-CMR acquisition:

LGE-CMR examinations were performed on 1.5 Tesla scanners (Achieva, Philips Medical System, Best, The Netherlands). A dedicated five-element, phase-array body coil was used. Images were acquired during repeated end-expiratory breath-old of 10-15 s, depending on the heart rate.

To evaluate myocardial thickness and global cardiac function, ECG-gated cine images were then acquired using Balanced Turbo Field Echo (b-TFE) sequence (Fig. 2).

Subsequently, LGE-CMR images were obtained in the same long and short axis orientation, 15 minutes after intravenous administration of 0.1 mmol/kg Gd-DOTA based contrast agent (Dotarem, Guerbet S.A., Cedex, France), using a breath-hold 3D Inversion-Recovery Turbo Field Echo (IR-TFE-3D) sequence acquired in the same views as the cine images (Fig. 3). The inversion recovery time was adjusted per patient to optimally null the signal from normal myocardium (typically 230-350 ms) [6].

Total acquisition time averaged 40 minutes.

Images analysis, determination of ventricular and atrial parameters and LGE quantification:

Cine and contrast-enhanced images were evaluated separately by the consensus of two observers who were unaware of the results of the other modality.

Volume and mass measurements were obtained by applying the Simpson's method with a dedicated software (ViewForum 3.2, Philips Medical System, Best, The Netherlands). All volumes and mass measurements were indexed to body surface area [7]
In addition to volumetric measurements, one dimensional measurements of left ventricular end diastolic dimensions, posterior wall thickness, and maximum inter-ventricular septum wall thickness were measured from ED short axis views [8].

The LGE was assessed automatically on short-axis slices by 2 observers blinded to all patient details. The mean signal intensity (and SD) of normal myocardium is calculated and a threshold # 6 SD exceeding the mean is used to define areas of LGE. Such quantitative scar analysis has been shown to be highly reproducible in a previous study [9]. Total volume of LGE (measured in grams) is expressed as a proportion of total LV myocardium mass (LGE%/ total myocardial mass) (Fig. 4).

**Electrocardiographic analysis and arrhythmia monitoring:**

The occurrence of VT or any other arrhythmia was documented by performing 24 h ECG Holter-monitoring. Presence of VT (sustained or non-sustained), was defined as: three or more consecutive ventricular beats at a rate of 120 beats/ min [6].

**Follow up**

All patients underwent successfully CMR examination.

The follow up was 32,1±11,2 months.

Occurrence of VT (sustained and non-sustained), ICD implant and ICD shocks during 32.1±11.2 months follow-up were recorded by interviewing patients and their cardiologists.

Only new events from the time of recruitment were considered in the primary or secondary outcomes.

**Statistical analysis:**

The statistical correlations between extension of LGE and the occurrence of VT and ICD shock was performed with university and multivariate analysis. All results were considered statistically significant when p<0.05.
**Fig. 1:** Table with demographic and clinical parameters of the study population.

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**Fig. 2:** short and long axis images of a patient with HCM by using B-TFE sequence.

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**Fig. 3:** LGE images of a patient with HCM by using IR-TFE 3D sequence in the same short and long axis orientation.

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**Fig. 4:** LGE quantification in a short axis view, by using automatic method: endocardial contour is marked by green line, epicardial contour by yellow line. A threshold # 6 SD above the signal of a non enhanced myocardium area was used to define areas of LGE and LGE% of total LV mass was quantified by using a dedicated software.

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Results

The mean IEDLV mass was 89.8±28.5 g/m². LGE was found in the majority of patients (53 patients; 85.5%), although its extension was usually quite limited (7.0±7.4% of IEDLV mass; median 5.25%; range 0-34%) (Fig. 5).

The pattern of LGE was peculiar, occurring only in hypertrophied regions, predominantly involving the middle third of the ventricular wall in a patchy, multi-focal distribution.

Interestingly, almost all patients with myocardial scar had involvement at the anterior and inferior junctions of the interventricular septum (Fig. 6).

During the follow-up 20 (32.3%) presented Non-Sustained Ventricular Tachyarrhythmias (NSVT) and 9 (14.5%) presented SVT on 24 hours Holter-monitoring. Eight (12.9%) patients implanted ICD and 4 of them experienced one or more ICD shock. There was a statistically significant correlation between LGE extension and NSVT (P=0.001), SVT and ICDS.

Moreover we divided the study population in two groups, the first one without SVT, the second one with SVT: patients who presented SVT had significantly higher LGE%, compared to those without: 12.3±6.9% vs. 6.1±7.1%, P=0.009 (Fig. 7, 8).

Then we considered the different distribution of LGE% between patients with or without ICD shock and we found that patients who presented one or more ICDS had significantly higher LGE%, compared to those without any shocks: 16.6±5.7% vs. 6.4±7%, P=0.003 (Fig. 9, 10).
**Fig. 5:** Table with CMR parameters of the study population.

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**Fig. 6:** LGE pattern of a patient with Hypertrophic Cardiomyopathy. Note the involvement at the anterior and inferior junctions of the interventricular septum.

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### Fig. 7: Table with CMR parameters in patients with and without SVT.

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**Fig. 8:** Relation between LGE extension and SVT.

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**Fig. 9:** Table with LGE extension in patients with or without ICD shock.

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Fig. 10: Relation between LGE extension and ICD shock.

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Conclusion

Extension of LGE predicts the occurrence of SVT and ICD shock in HCM patients.

These findings underline the potential predictive value of LGE-CMR to stratify patients with HCM by risk of arrhythmic events.

Therefore, the use of LGE-CMR may be relevant to influence therapeutic strategies, in particular to clinical decision making and considerations for prophylactic ICD therapy in selected patients with HCM.
References


