

Late gadolinium enhancement is common in patients with hypertrophic cardiomyopathy and no clinical risk factors for sudden cardiac death: A single center experience

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Abstract

Background: Cardiac magnetic resonance (CMR) is used in the diagnosis and risk stratification of hypertrophic cardiomyopathy (HCM) and can detect myocardial replacement fibrosis (an independent predictor of adverse cardiac outcomes) using late gadolinium enhancement (LGE).

Methods: We retrospectively analysed CMR studies carried out over a 2 year period identifying those which were diagnostic of HCM. 117 cases were analysed. Mean age of subjects was 53 years and 78 (67%) were male. Mean ejection fraction (EF) was 68.3% with a mean left ventricular (LV) mass index of 89.4 g/m². Hypertrophy was predominantly asymmetric in 94 (80%).

Results: All subjects received gadolinium and 80 (68%) had evidence of LGE. LVEF was lower (67 vs. 71%; $p = 0.015$) and LV mass index higher (94 vs. 81 g/m²; $p = 0.007$) in the LGE group. The proportion of patients with at least 1 clinical risk factor for sudden cardiac death (SCD) was similar in groups with and without LGE (48% vs. 32%; $p = 0.160$). In this study, a significant proportion (62%) of patients without clinical risk factors for SCD were found to have LGE on CMR. These patients would not currently be considered for therapy with an implantable cardiac defibrillator.

Conclusions: 1. Patients with HCM are at increased risk of SCD, but identifying patients who may benefit from implantable defibrillators is difficult. 2. LGE is associated with adverse cardiovascular outcomes in HCM, but is present in a large proportion of patients. 3. Many patients without clinical risk factors for SCD have LGE and would not currently be considered for an implantable cardiac device. (Cardiol J 2014; 21, 1: 29–32)

Key words: hypertrophic cardiomyopathy, cardiac magnetic resonance, sudden cardiac death, late gadolinium enhancement

Introduction

Cardiac magnetic resonance (CMR) is now widely used in the diagnosis and risk stratification of hypertrophic cardiomyopathy (HCM). It has

several advantages over echocardiography including more accurate measurement of left ventricular function and mass, and it aids in the identification of apical HCM variants and alternative causes of hypertrophy such as athlete's heart and Fabry's

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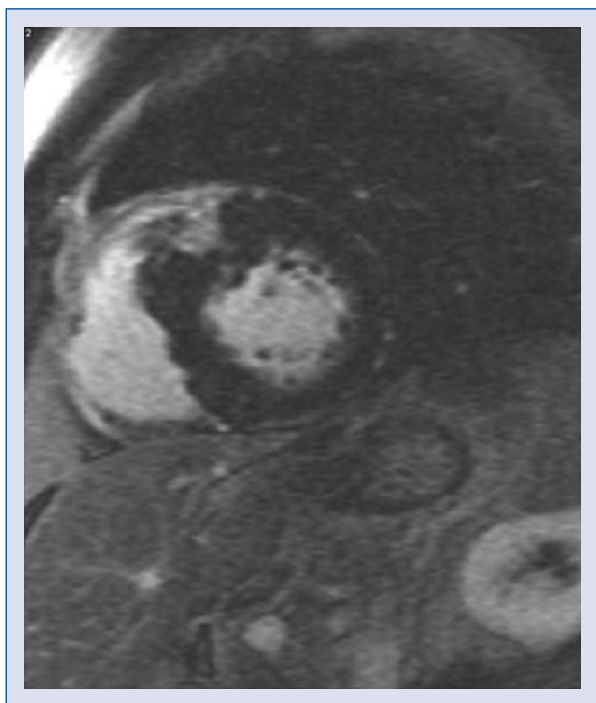


Figure 1. Late gadolinium enhancement within the interventricular septum in a patient with hypertrophic cardiomyopathy.

diseases. Furthermore, it has the ability to demonstrate areas of myocardial replacement fibrosis using late gadolinium enhancement (LGE) (Fig. 1) which is increasingly being recognised as an independent predictor of adverse cardiac outcomes [1–6]. Several recently published reports have found an increased incidence of adverse cardiovascular events in patients with LGE compared to those without, and the sensitivity of clinical risk factors for prediction of sudden cardiac death (SCD) has been questioned. However previous studies have shown that LGE is present in a large proportion of patients with HCM, and therefore identifies too large a population to be useful as a single predictor. We sought to look at the occurrence of LGE in our population and assess the association of LGE with clinical risk factors.

Methods

We performed a retrospective analysis of all CMR studies carried out in a single center over a 24 month period from January 2010 to December 2011. Data was collected on all patients in whom CMR findings were consistent with a diagnosis of HCM ie. a hypertrophied and non-dilated ventricle in the absence of another condition capable of producing the observed degree of hypertrophy [7]. A cut-off for maximal wall thickness of 15 mm

was used in adults in keeping with current guidelines although some patients with maximal wall thickness less than 15 mm were included if there was a strong clinical suspicion of HCM based on a family history of the condition in at least one first degree relative. Patients who had left ventricular (LV) hypertrophy which was potentially due to another condition such as hypertension were excluded, as were patients who did not receive a gadolinium based contrast agent as part of the imaging protocol.

All studies were performed on a Siemens Avanto 1.5 T scanner. LGE images were obtained after administration of intravenous gadobenate demeglumine (0.2 mmol/kg). LV function and mass were analysed after manual identification of endocardial and epicardial borders. The amount of LGE was not measured quantitatively but was noted to be present or absent.

Patient demographics and occurrence of clinical risk factors for SCD were obtained from review of clinical notes. CMR findings were taken from reports by level II or III accredited cardiologists. LV mass and function (indexed), distribution of hypertrophy and the presence of systolic anterior motion of the mitral valve (SAM) or elevated LV outflow tract (LVOT) velocities were noted.

As this was a retrospective analysis of patient records and no additional procedures beyond normal patient care were carried out, ethical approval and patient consent were not required.

Statistical analysis

Statistical analysis was carried out using SPSS v.17.0. Categorical variables were compared using χ^2 test. Continuous variables were compared using the independent students *t*-test.

Results

One hundred and seventeen cases were included for analysis. Mean age of subjects was 53 ± 15.8 years and 78 (67%) were male. Mean ejection fraction (EF) was $68.3 \pm 8.5\%$ with a mean LV mass index of 89.4 ± 26.7 g/m². SAM was present in 24 (21%) and 16 (14%) had an elevated LVOT velocity. The pattern of hypertrophy was predominantly asymmetric in 94 (80%), predominantly apical in 13 (11%) and concentric in 10 (9%).

All subjects received gadolinium and some degree of LGE was present in 80 (68%). There was no significant difference in prevalence of LGE based on gender ($p = 0.115$). LGE was more common in apical (79%) and concentric (80%) patterns of hypertrophy compared to asymmetric (65%) although this difference was not statistically significant

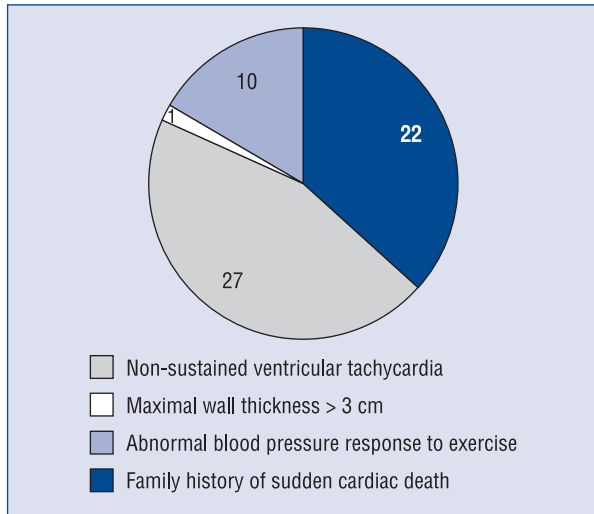


Figure 2. Frequency of individual clinical risk factors in the study group.

($p = 0.254$). LVEF was lower ($67 \pm 8.5\%$ vs. $71 \pm 8.0\%$; $p = 0.015$) and LV mass index higher ($94 \pm 27.9 \text{ g/m}^2$ vs. $81 \pm 21.7 \text{ g/m}^2$; $p = 0.007$) in the LGE group.

Fifty (43%) of the 117 patients had at least 1 clinical risk factor for SCD. The frequency of individual risk factors is shown in Figure 2. The percentage of patients with clinical risk factors in the LGE and no LGE groups is shown in Table 1. Only the difference in non sustained ventricular tachycardia (NSVT) between groups was statistically significant ($p = 0.035$).

Discussion

The risk stratification of patients with HCM is complex. Current guidelines recommend that an implantable cardiac defibrillator be considered in patients with 1 or more clinical risk factors for SCD [7]. However there is mounting evidence that

LGE may be a much more specific predictor of poor prognosis in this condition, with adverse events being uncommon in patients without LGE [4]. The findings of this study are similar to previous reports, with regard to the proportion of patients with evidence of LGE [3]. In our group LGE was present in 68% of patients with HCM. However, when a risk factor is present in such a large proportion of patients, further discriminators are required to improve predictive power. These may include factors such as LV mass and quantification of LGE as a percentage of myocardial mass, with higher percentage correlating with greater risk [4].

Traditional risk factors for SCD were present in 50 (43%) patients. Although NSVT was statistically more common in patients with LGE, overall the presence of any risk factor was not, suggesting that LGE is not simply a marker of commonly assessed clinical risk factors. A significant proportion of patients (63%) without traditional clinical risk factors for SCD were found to have LGE on CMR and these patients would not currently be considered for therapy with an implantable cardiac defibrillator. The use of clinical risk factors in everyday practice presents several problems. Maximal wall thickness > 3 cm is present in a very small number of patients (only 1 in this study). Blood pressure response to exercise may be difficult to assess in many patients with mobility problems and can be unreliable in patients over 50 years of age [8]. Even family history of SCD may be difficult to quantify in patients who are unaware of their extended family tree. This study found that a significant proportion of patients with HCM who do not have clinical risk factors have evidence of LGE on CMR and may still be at increased risk of SCD. CMR with LGE provides a method of assessing myocardial replacement fibrosis and with further modification may be the most sensitive means of identifying patients at risk for cardiovascular events.

Table 1. Occurrence of clinical risk factors for SCD according to presence or absence of LGE.

	Late gadolinium enhancement	No late gadolinium enhancement	P
0 risk factors	42 (63%)	25 (37%)	0.160
≥ 1 risk factor	38 (48%)	12 (32%)	0.160
Family history of SCD	17 (21%)	5 (14%)	0.447
NSVT on Holter	23 (29%)	4 (11%)	0.035
Abnormal stress test	7 (9%)	3 (8%)	1.000
Maximal wall thickness ≥ 3 cm	1 (1%)	0 (0%)	1.000

LGE — late gadolinium enhancement; SCD — sudden cardiac death; NSVT — non sustained ventricular tachycardia

Limitations of the study

This study has several limitations which must be considered. This is a retrospective analysis however for the purposes of assessing the relationship between LGE and clinical risk factors, a restrospective design was thought to be a reasonable approach. No endpoint data was therefore acquired (with regard to cardiovascular events in the population). The extent of LGE was assessed qualitatively as currently our CMR software does not allow quantitative assessment, however qualitative analysis may allow more accurate assessment of risk. The small numbers of patients in some groups made analysis difficult, and may have contributed to a lack of association with LGE and clinical risk factors over all however the number of subjects was reasonable for a single centre study of this type and the frequency of risk factors reflects that in a real world population.

Conclusions

1. Patients with HCM are at increased risk of SCD, but identifying patients who may benefit from implantable defibrillators is difficult.
2. LGE is associated with adverse cardiovascular outcomes in HCM, but is present in a large proportion of patients.
3. Many patients without clinical risk factors for SCD have LGE and would not currently be considered for an implantable cardiac device.

Conflict of interest: none declared

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