High Signal Intensity on T2-Weighted Cardiovascular Magnetic Resonance Imaging Predicts Life-Threatening Arrhythmic Events in Hypertrophic Cardiomyopathy Patients

Yasuki Hen, MD; Ayako Takara, MD; Nobuo Iguchi, MD; Yuko Utanohara, MD; Kunihiro Teraoka, MD; Kaori Takada, MD; Haruhiko Machida, MD; Itaru Takamisawa, MD; Morimasa Takayama, MD; Tsutomu Yoshikawa, MD

Background: The prognostic value of high signal intensity on T2-weighted cardiovascular magnetic resonance imaging (T2 high signal) in hypertrophic cardiomyopathy (HCM) patients in a single-center cohort was investigated.

Methods and Results: A total of 237 HCM patients (median age, 62 years; 143 male) underwent T2-weighted, cine and late gadolinium enhancement (LGE) imaging, and were followed (median duration, 3.4 years) for life-threatening arrhythmic events. The clinical and magnetic resonance imaging characteristics were extracted, and predictors of life-threatening arrhythmic events were assessed on multivariate analysis. LGE was present in 180 patients (75.9%). Median LGE score was 3 in a left ventricle 17-segment model. T2 high signal was present in 49 patients (20.7%). The annual events rate was significantly higher in patients with extensive LGE (score ≥4) than in those without (3.0%/year vs. 0.5%/year, P=0.011). On multivariate analysis, extensive LGE (hazard ratio, 5.650; 95% CI: 1.263–25.000, P=0.024) as an independent predictor for life-threatening arrhythmic events. In patients with extensive LGE, the annual events rate was significantly higher in patients with T2 high signal than in those without (5.8%/year vs. 0.9%/year, P=0.008).

Conclusions: Extensive LGE was an independent predictor of life-threatening arrhythmic events in HCM patients. Furthermore, T2 high signal is useful for the risk stratification of serious arrhythmic events in patients with extensive LGE.

Key Words: Cardiac magnetic resonance; Hypertrophic cardiomyopathy; Late gadolinium enhancement; Life-threatening arrhythmic event; T2-weighted imaging

Prevention of sudden cardiac death (SCD) is an important issue for patients with hypertrophic cardiomyopathy (HCM). Although implantable cardioverter defibrillator (ICD) is an effective preventive therapy for SCD,1,2 the indications for this therapy for primary prevention remain an unsolved question. In recent years, many reports have described the relationship between late gadolinium enhancement (LGE) on cardiovascular magnetic resonance imaging (CMR) and the prognosis of SCD in HCM patients.3,9 and LGE is expected to be useful in deciding indication for ICD implantation. There are some differences between the current Japanese guidelines and European or US guidelines on ICD implantation for primary prevention in patients with HCM.10,12 LGE on CMR is mentioned in the 2011 US guidelines only under “other potential SCD risk modifiers”,10 while LGE is not yet included as a risk assessment factor in European and Japanese guidelines.11,12

In contrast, given that myocardial edema is visualized as high signal intensity (SI) on CMR T2-weighted imaging (T2WI),13 this is considered useful for the diagnosis of myocarditis and takotsubo cardiomyopathy as well as for the evaluation of the salvaged area in acute myocardial infarction (MI).14,18 In previous studies some HCM patients also had high SI on T2WI (T2 high signal).19–27 Although we have previously reported that T2 high signal is an independent predictor of ventricular tachyarrhythmia,22 there is no report on the prognostic significance of T2 high signal to predict life-threatening arrhythmic events. The aim of this study was therefore to validate the significance of T2 high signal as a prognostic factor in predicting life-threatening arrhythmic events in a relatively large number of HCM patients who underwent gadolinium enhanced imaging and T2WI.
Methods

Patient Selection
We conducted a retrospective study on 237 HCM patients who underwent T2WI and gadolinium contrast-enhanced CMR between January 2008 and December 2010. First, we explained to all the patients that their clinical data were to be used in a retrospective study through the Sakakibara Heart Institute (SHIP) database, and then obtained written informed consent from the patients. This study was approved by the Ethics Committee of Sakakibara Heart Institute (13-007). HCM was defined as left ventricular (LV) wall thickness ≥15 mm on echocardiography and/or CMR, in the absence of other cardiac or systemic diseases that could account for the hypertrophy. Patients who were already diagnosed with HCM before undergoing CMR were recruited into this study even with LV wall thickness <15 mm. To investigate the prognosis of HCM, patients with old MI, those who had concurrent congenital heart disease, those with severe valvular disease (including those who had undergone surgery for valvular diseases), and those who had undergone percutaneous transluminal septal myocardial ablation (PTSMA) or septal myectomy before CMR were excluded.

CMR Protocols and Imaging
CMR was performed with a 1.5-T MR scanner (Magnetom Sonata; Siemens Medical Solutions, Erlangen, Germany) using a 6-channel phased-array body and spine coil. All images were acquired using the electrocardiography (ECG)-gated breath-hold technique. First, steady-state free-precession cine images were acquired in 3 long-axis (2-, 3-, and 4-chamber) and short axis views covering the LV from base to apex (TR, 56.8 ms; TE, 1.2 ms). Subsequently, black-blood T2-weighted multi-echo spin-echo imaging with fat suppression (short tau inversion recovery) was acquired (TR, 2 heartbeats; TE, 104 ms; TI, 170 ms; field of view, 340 mm; matrix, 192×256; slice thickness, 8 mm; echo-train length, 21; bandwidth, 399 Hz/pixel) in the same views used in cine imaging. Finally, LGE images were acquired 10 min after i.v. gadoximate hydrate (Omniscan; Daiichi Sankyo, Tokyo, Japan), using the inversion recovery technique in the identical views (TR, 600 ms; TE, 1.26 ms; TI was individually optimized to null normal myocardial signal using a TI-scout sequence).

Two cardiologists, in consensus, visually evaluated LGE imaging for the presence or absence of LGE within the LV myocardium for each patient. The extent of LGE was assessed using the LV 17-segment model (Figure 1). The extent of LGE was scored on a scale of 0–17, as the sum of the segments in the 17-segment model with LGE.

Furthermore, we visually evaluated T2WI for the presence or absence of T2 high signal within the LV myocardium for each patient. We measured the mean SI and SD at the brightest myocardium and reference myocardium using Picture Archiving and Communication System (INFINITT). A square ≥2.5×2.5 mm region of interest (ROI) was placed in the myocardium without overlapping the endocardial and epicardial borders to exclude artifacts. The presence of T2 high area was confirmed when the mean SI was greater than mean SI+3 SD of a reference myocardium (myocardial area without bright and dark signal) on T2WI.

There is no established definition of T2 high signal evaluation for HCM patients, but the clinical significance of T2 high has been reported using 2–3-SD methods. We evaluated the threshold of T2 high signal at 3 SD. Maximum LV wall thickness was determined by measuring the minimum thickness of the thickest LV myocardium in the cine image at end-diastole.

Clinical and CMR Status and Outcome
The clinical records of all 237 patients were reviewed, and the clinical findings and medication at the time of CMR were extracted. Low blood pressure during exercise was not included in analysis because the exercise test was performed in very few study patients. Ventricular tachycardia (VT) was defined as heart rate ≥120 beats/min for ≥3 consecutive beats. In all 237 patients, the occurrence of cardiovascular events as of August 2015 was determined retrospectively from clinical records. Life-threatening arrhythmic events were defined as sudden death, aborted sudden death, sustained VT/ventricular fibrillation (VF), appropriate ICD discharge for VT/VF. The length of follow-up was until the most recent follow-up or death. For patients who underwent de novo PTSMA, surgical septal myectomy, or valve replacement during the follow-up period, the time at which these alternative endpoints occurred was regarded as the end of follow-up. During the follow-up period, PTSMA was performed in 66 patients (28%) and surgical septal myectomy in 2 patients.

Statistical Analysis
Data are expressed as mean±SD, median (IQR) or n (%) as appropriate. Differences between medians were tested using Mann-Whitney U-test. Categorical variables were compared using chi-squared test or Fisher’s exact test, as appropriate. Event-free rates from life-threatening arrhythmia were calculated according to the Kaplan-Meier method and were compared using log-rank test. Univariate Cox proportional hazards regression analysis was performed using the clinical, echocardiographic, and CMR variables considered possibly related to life-threatening arrhythmic events. For multivariate analysis, those variables with P<0.05 on univariate analysis were entered into the model. Furthermore, the multivariate model was constructed using a stepwise selection method with entrance...
and stay criteria. P<0.05 was considered to be statistically significant. Statistical analysis was performed using SPSS ver. 20.0.

Results

Clinical and CMR Characteristics

Table 1 lists the clinical characteristics of 237 HCM patients. Median age was 62 years old. Regarding the conventional risk factors, family history of SCD was identified in 25 patients (10.5%), history of syncope in 36 patients (15.2%) and VT in 43 patients (18.1%), and maximum wall thickness ≥30 mm in 26 patients (11.0%). Atrial fibrillation was identified in 36 patients (15.2%). Median LV ejection fraction (EF) was 68.3%. Intraventricular pressure gradient ≥30 mmHg, indicating obstructive HCM, was present in 106 patients (44.7%). Beta-blocker was given in 156 patients (65.8%) and calcium antagonist in 64 patients (27.0%), and class I anti-arrhythmics (cibenzoline or disopyramide) in 85 patients (35.9%). LGE was present in 180 patients (75.9%). Median LGE score was 3.

We classified the 237 study patients into 2 groups with or without extensive LGE (LGE ≥4, LGE ≤3). The cut-off of LGE score was defined as the median LGE score. Extensive LGE was present in 105 patients (44.3%). T2 high signal was present in 49 patients overall (20.7%). With regard to LGE status, T2 high signal was present in 45 of 105 patients (42.9%) with extensive LGE, and in only 4 of 132 patients (3.0%) without extensive LGE.

Figure 2 shows LGE imaging (upper panel) and T2WI (lower panel) in 2 different patients (A,B). Both patients had extensive LGE. Myocardial T2-high signal areas (white arrow) were detected in patient A with appropriate implantable cardioverter defibrillator discharge for VT at 4 months after CMR. In contrast,
Figure 3. Kaplan-Meier life-threatening arrhythmic event-free cumulative survival curves according to late gadolinium enhancement (LGE) status. Blue line, extensive LGE negative; red line, extensive LGE positive. CMR, cardiac magnetic resonance imaging.

Figure 4. Kaplan-Meier life-threatening arrhythmic event-free cumulative survival curves according to high signal intensity on T2-weighted cardiovascular magnetic resonance imaging (CMR; T2 high signal), in patients with extensive late gadolinium enhancement. Blue line, T2 high signal negative; red line, T2 high signal positive.
HEN Y et al.

Extensive LGE, we compared clinical outcome in patients with extensive LGE according to T2 high signal status. In patients with extensive LGE, life-threatening arrhythmic events occurred at a higher rate in patients with T2 high signal than in those without T2 high signal (annual events rate, 5.8%/year vs. 0.9%/year, $P=0.008$, Figure 4).

Predictors for Life-Threatening Arrhythmic Events

Table 2 lists the results of Cox proportional hazards regression analysis. First, we performed univariate analysis using variables presumed to be correlated with life-threatening arrhythmic events. On univariate analysis, age, VT, LVEF, maximum LV wall thickness, and extensive LGE were significantly associated with life-threatening arrhythmic events ($P<0.05$). These variables were then entered into the multivariate analysis.

Follow-up Results

We examined life-threatening arrhythmic events until August 2015 (median follow-up, 3.4 years). During the follow-up period, life-threatening arrhythmic events occurred in 14/237 patients (5.9%; sudden death in 2, aborted sudden death in 3, appropriate ICD discharge for VT/VF in 9). On Kaplan-Meier survival analysis, compared with patients without extensive LGE (LGE score $\leq 3$), those with extensive LGE (LGE score $\geq 4$) had a higher life-threatening arrhythmic event rate (annual events rate, 3.0%/year vs. 0.5%/year, $P=0.011$; Figure 3). Given that T2 high signal was observed in very few HCM patients without extensive LGE, we compared clinical outcome in patients with extensive LGE according to T2 high signal status. In patients with extensive LGE, life-threatening arrhythmic events occurred at a higher rate in patients with T2 high signal than in those without T2 high signal (annual events rate, 5.8%/year vs. 0.9%/year, $P=0.008$, Figure 4).

T2-high signal areas were not detected in patient B without life-threatening arrhythmic events.

### Table 2. Indicators of Life-Threatening Arrhythmic Events in HCM Patients

| Variable                          | Univariate analysis | Multivariate analysis |
|-----------------------------------|---------------------|-----------------------|
|                                  | Unadjusted HR | 95% CI | P-value | Adjusted HR | 95% CI | P-value |
| Age (years)                       | 0.970            | 0.944–0.996        | 0.026    |             |        |        |
| Male                              | 1.613            | 1.447–5.814        | 0.465    |             |        |        |
| Family history of HCM             | 1.942            | 0.541–6.970        | 0.308    |             |        |        |
| Family history of SCD             | 1.259            | 0.281–5.650        | 0.763    |             |        |        |
| History of syncope                | 0.604            | 0.079–4.630        | 0.828    |             |        |        |
| VT                                | 2.941            | 1.029–8.403        | 0.044    |             |        |        |
| AF                                | 1.299            | 0.362–4.664        | 0.688    |             |        |        |
| NYHA functional class III or IV   | 1.589            | 0.208–12.170       | 0.656    |             |        |        |
| β-blocker                         | 1.134            | 0.380–3.390        | 0.822    |             |        |        |
| Calcium antagonist                | 0.227            | 0.030–1.734        | 0.153    |             |        |        |
| Anti-arrhythmics (class I)        | 0.540            | 0.195–1.494        | 0.235    |             |        |        |
| Pressure gradient ≥30mmHg         | 1.582            | 0.527–4.762        | 0.413    |             |        |        |
| LVEF (%)                          | 0.962            | 0.931–0.994        | 0.019    |             |        |        |
| Maximum LV wall thickness (mm)    | 1.113            | 1.021–1.212        | 0.014    |             |        |        |
| Extensive LGE (LGE score ≥4)      | 5.642            | 1.262–25.222       | 0.024    | 5.650       | 1.263–25.000 | 0.024 |

### Table 3. Indicators of Life-Threatening Arrhythmic Events in HCM Patients With Extensive LGE

| Variable                          | Univariate analysis | Multivariate analysis |
|-----------------------------------|---------------------|-----------------------|
|                                  | Unadjusted HR | 95% CI | P-value | Adjusted HR | 95% CI | P-value |
| Age (years)                       | 0.983            | 0.955–1.012        | 0.248    |             |        |        |
| Male                              | 3.460            | 0.445–27.027       | 0.236    |             |        |        |
| Family history of HCM             | 1.786            | 0.483–6.623        | 0.385    |             |        |        |
| Family history of SCD             | 1.107            | 0.242–5.068        | 0.896    |             |        |        |
| History of syncope                | 0.040            | 0.000–66.667       | 0.398    |             |        |        |
| VT                                | 1.575            | 0.506–4.902        | 0.433    |             |        |        |
| AF                                | 1.280            | 0.346–4.739        | 0.712    |             |        |        |
| NYHA functional class III or IV   | 1.176            | 0.160–9.615        | 0.838    |             |        |        |
| β-blocker                         | 1.972            | 0.532–7.299        | 0.310    |             |        |        |
| Calcium antagonist                | 0.284            | 0.037–2.203        | 0.228    |             |        |        |
| Anti-arrhythmics (class I)        | 0.375            | 0.048–2.917        | 0.349    |             |        |        |
| Pressure gradient ≥30mmHg         | 1.036            | 0.280–3.846        | 0.957    |             |        |        |
| LVEF (%)                          | 0.961            | 0.928–0.996        | 0.027    |             |        |        |
| Maximum LV wall thickness (mm)    | 1.048            | 0.952–1.154        | 0.337    |             |        |        |
| T2 high signal                    | 6.061            | 1.325–27.778       | 0.020    | 6.061       | 1.325–27.778 | 0.020 |

Abbreviations as in Table 1.
Discussion

In this study, we investigated the prognostic impact of T2 high signal in addition to LGE in a large series of HCM patients using CMR. T2 high signal was observed in very few HCM patients without extensive LGE. In patients with extensive LGE, the presence of T2 high signal was independently associated with life-threatening arrhythmic events on long-term follow-up.

Prevention of SCD is a crucial issue in HCM patients. Although ICD is currently an effective tool to prevent SCD, prediction of SCD per se remains to be determined. In HCM, given that SCD prevention is required even in relatively young patients, the use of ICD may span long periods of time. Also, given the long-term ICD-related complications, it is currently difficult to decide on ICD implantation for primary prevention.

Conventionally, indication for ICD implantation for primary prevention is decided based on evaluation of 5 conventional risk factors for SCD, but, although LGE is commonly observed in HCM patients using CMR, T2 high signal was observed in very few HCM patients without extensive LGE. In patients with extensive LGE, the presence of T2 high signal was independently associated with life-threatening arrhythmic events on long-term follow-up.

Extensive LGE has also been observed in some patients with HCM. In those studies, perfusion imaging showed greatly reduced myocardial blood flow in the T2 high signal region compared with other regions, and cardiac troponin T and/or brain natriuretic peptide was elevated in HCM patients with T2 high signal.

In a recent report, 5-year SCD risk was estimated in 109 HCM patients according to the European or North American guidelines. HCM patients with T2 high signal were more often at intermediate-high risk of SCD in that analysis. We previously reported that T2 high signal was frequently observed in patients with non-sustained VT. The present study is the first to examine whether T2 high signal is a prognostic determinant.

Extensive LGE has also been suggested to be an arrhythmogenic source of ventricular arrhythmia. In contrast, there are subtle differences in the LGE SI in HCM patients. Areas with lesser LGE SI are composed of substantial tissue heterogeneity, including a mixture of intact myocytes and fibrosis. With regard to LGE SI, intermediate rather than high SI was a stronger predictor of non-sustained VT, suggesting that tissue heterogeneity is associated with arrhythmogenic source. Although T2 high signal tends to overlap with the LGE areas, we speculate that T2 high signal may reflect tissue heterogeneity within the LGE areas. Furthermore, it was hypothesized that T2 high signal in HCM may indicate active, ongoing tissue injury because of elevated cardiac troponin T. Considering tissue heterogeneity and ongoing tissue injury, life-threatening arrhythmic events may occur at a high rate in patients with both T2 high signal and extensive LGE.

In the present study, we showed that extensive LGE was an independent predictor of life-threatening arrhythmic events in HCM patients. Furthermore, we focused on patients with extensive LGE, and compared the prognosis...
according to T2 high signal status. Adverse prognosis was noted in patients with T2 high signal compared with those without T2 high signal. This indicates that combining gadolinium-enhanced imaging with T2WI is useful for risk stratification of life-threatening arrhythmic events in patients with HCM.

**Study Limitations**
There were several limitations in this study. First, the study was a retrospective, single-center study conducted in a tertiary hospital. Second, LGE evaluation was conducted visually, and was semi-quantitative. Finally, the universal definition of T2 high signal remains to be determined. In the present study, in accordance with previous reports, positive T2 high signal was defined as SI ≥2–3 SD above that of the reference myocardium.22–27 T2-mapping sequences have also been used for the high signal area.28 Further verification is necessary in the future. To resolve these limitations, it would be necessary to carry out a prospective follow-up CMR study using quantitative and standardized evaluation of LGE and T2 high signal.

**Conclusions**
In 237 patients with HCM, extensive LGE was an independent predictor of life-threatening arrhythmic events. Furthermore, T2 high signal was useful for the risk stratification of serious arrhythmic events in patients with extensive LGE.

**Acknowledgments**
This study was supported by the Sakakibara Clinical Research Grant for Promotion of Science, 2017. We gratefully thank Mr Naokazu Mizuno and Mr Jun Matsuda at Sakakibara Heart Institute for technical assistance.

**Disclosures**
The authors declare no conflict of interest.

**References**
1. Maron BJ, Shen WK, Epstein AE, Almquist AK, Daubert JP, et al. Efficacy of implantable cardioverter-defibrillators for the prevention of sudden death in patients with hypertrophic cardiomyopathy. *N Engl J Med* 2000; 342: 365–373.
2. Maron BJ, Spira P, Shen WK, Haas TS, Formisano F, Link MS, et al. Implantable cardioverter-defibrillators and prevention of sudden cardiac death in hypertrophic cardiomyopathy. *JAMA* 2007; 298: 405–412.
3. Rubinstein R, Gloekler JF, Ommen SR, Araoz PA, Ackerman MJ, Soraja P, et al. Characteristics and clinical significance of late gadolinium enhancement by contrast-enhanced magnetic resonance imaging in patients with hypertrophic cardiomyopathy. *Circ Heart Fail* 2010; 3: 51–58.
4. Bruder O, Wagner A, Jensen CJ, Schneider S, Ong P, Kispert EM, et al. Myocardial scar visualized by cardiovascular magnetic resonance imaging predicts major adverse events in patients with hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2010; 56: 875–887.
5. Hen Y, Iguchi N, Utanohara Y, Takada K, Machida H, Takayama M, et al. Prognostic value of late gadolinium enhancement on cardiac magnetic resonance imaging in Japanese hypertrophic cardiomyopathy patients. *Circ J* 2014; 78: 929–937.
6. Ismail TF, Jabbour A, Gulati A, Mallorie A, Raza S, Cowling TE, et al. Role of late gadolinium enhancement cardiovascular magnetic resonance in the risk stratification of hypertrophic cardiomyopathy. *Heart* 2014; 100: 1851–1858.
7. Chan RH, Maron BJ, Olivotto I, Pencina MJ, Assenza GE, Haas T, et al. Prognostic value of quantitative contrast-enhanced cardiovascular magnetic resonance for the evaluation of sudden death risk in patients with hypertrophic cardiomyopathy. *Circulation* 2014; 130: 484–495.
associated with elevated troponin T in hypertrophic cardiomyopathy. *Heart* 2017; **103**: 293–299.

28. Hen Y, Iuchi N, Utanohara Y, Takada K, Machida H, Takara A, et al. Extent of late gadolinium enhancement on cardiac magnetic resonance imaging in Japanese hypertrophic cardiomyopathy patients. *Circ J* 2016; **80**: 950–957.

29. Cerqueira MD, Weissman NJ, Dilsizian V, Jacobs AK, Kaul S, Laskey WK, et al. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart: A statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. *Circulation* 2002; **105**: 589–610.

30. Lin G, Nishimura RA, Gersh BJ, Phil D, Ommen SR, Ackerman MJ, et al. Device complications and inappropriate implantable cardioverter defibrillator shocks in patients with hypertrophic cardiomyopathy. *Heart* 2009; **95**: 709–714.

31. O’Mahony C, Lambiase PD, Quarta G, Cardona M, Calcagnino M, Tsivolas K, et al. The long-term survival and the risks and benefits of implantable cardioverter defibrillators in patients with hypertrophic cardiomyopathy. *Heart* 2012; **98**: 116–125.

32. Schinkel AF, Vreesendorp PA, Sjibrands EF, Jordaan LJ, ten Cate FJ, Michels M. Outcome and complications after implantable cardioverter defibrillator therapy in hypertrophic cardiomyopathy: Systematic review and meta-analysis. *Circ Heart Fail* 2012; **5**: 552–559.

33. Elliott PM, Poloniecki J, Dickie S, Sharma S, Monserrat L, Varnava A, et al. Sudden death in hypertrophic cardiomyopathy: Identification of high risk patients. *J Am Coll Cardiol* 2000; **36**: 2212–2218.

34. Christians A, van Engelen K, van Langen IM, Birnie E, Bonsel GJ, Elliott PM, et al. Risk stratification for sudden cardiac death in hypertrophic cardiomyopathy: Systematic review of clinical risk markers. *Europace* 2010; **12**: 313–321.

35. Spirito P, Autore C, Formisano F, Assenza GE, Biagini E, Haas TS, et al. Risk of sudden death and outcome in patients with hypertrophic cardiomyopathy with benign presentation and without risk factors. *Am J Cardiol* 2014; **113**: 1550–1555.

36. O’Mahony C, Jichi F, Pavlou M, Monserrat L, Anastasakis A, Raperze C, et al. A novel clinical risk prediction model for sudden cardiac death in hypertrophic cardiomyopathy (HCM Risk-SCD).

37. Maron BJ, Casey SA, Chan RH, Garberich RF, Rowin EJ, Maron MS. Independent assessment of the European Society of Cardiology sudden death risk model for hypertrophic cardiomyopathy. *Am J Cardiol* 2015; **116**: 757–764.

38. Maron BJ, Ommen SR, Semsarian C, Spirito P, Olivotto I, Maron MS. Hypertrophic cardiomyopathy: Present and future, with translation into contemporary cardiovascular medicine. *J Am Coll Cardiol* 2014; **64**: 83–99.

39. Moon JC, Reed E, Sheppard MN, Elkington AG, Ho SY, Burke M, et al. The histologic basis of late gadolinium enhancement cardiovascular magnetic resonance in hypertrophic cardiomyopathy. *Am J Cardiol* 2004; **93**: 2260–2264.

40. Papavassiliu T, Schnabel P, Schroder M, Borggrefe M. CMR scarring in a patient with hypertrophic cardiomyopathy correlates well with histological findings of fibrosis. *Eur Heart J* 2005; **26**: 2395.

41. Knaapen P, van Dockum WG, Bondarenko O, Kok WE, Gotte MJ, Boellaard R, et al. Delayed contrast enhancement and perfusable tissue index in hypertrophic cardiomyopathy: Comparison between cardiac MRI and PET. *J Nucl Med* 2005; **46**: 923–929.

42. Aso H, Takeda K, Ito T, Shiraishi T, Matsumura K, Nakagawa T. Assessment of myocardial fibrosis in cardiomyopathic hamsters with gadolinium-DTPA enhanced magnetic resonance imaging. *Invest Radiol* 1998; **33**: 22–32.

43. Basso C, Thiene G, Corrado D, Buja G, Melacini P, Nava A. Hypertrophic cardiomyopathy and sudden death in the young: Pathologic evidence of myocardial ischemia. *Hum Pathol* 2000; **31**: 988–998.

44. Gommans DHF, Cramer GE, Bakker J, Dieker HJ, Michels M, Fouraux MA, et al. High T2-weighted signal intensity for risk prediction of sudden cardiac death in hypertrophic cardiomyopathy. *Int J Cardiovasc Imaging* 2018; **34**: 113–120.

45. Appelbaum E, Maron BJ, Adabag S, Hauser TH, Lesser JR, Haas TS, et al. Intermediate-signal-intensity late gadolinium enhancement predicts ventricular tachyarrhythmias in patients with hypertrophic cardiomyopathy. *Circ Cardiovasc Imaging* 2012; **5**: 78–85.