

# **Enhancing Risk Prediction for Sudden Cardiac Death: Quantitative Late Gadolinium Enhancement Analysis in Hypertrophic Cardiomyopathy**

## **Electronic Supplementary Materials**

### **Supplemental methods**

#### **CMR image acquisition**

All CMR examinations were performed on 3.0 T scanners (Discovery MR750, GE medical systems; MAGNETOM Verio, Siemens Healthineers; Ingenia, Philips) using standardized cardiac protocols with electrocardiographic gating and breath-holding. Standard CMR protocols mainly consisted of (1) Balanced steady-state free precession cine sequences were acquired in the LV long-axis (two-, three-, and four-chamber views) as well as in a stack of short-axis slices covering the entire left ventricle; (2) LGE images were performed by 2-dimensional segmented phase-sensitive inversion-recovery sequences in the same views as the cine images, approximately 10-15 min after the intravenous administration of either gadopentetate dimeglumine (0.2 mmol/kg; Magnevist, Bayer Healthcare Pharmaceuticals) or gadobutrol (0.1 mmol/kg; Gadavist, Bayer Healthcare Pharmaceuticals).

#### **Intra- and inter-observer agreement**

Intra- and inter-observer agreement for LGE quantification were assessed in 30 randomly selected cases. For intra-observer variability, measurements were repeated by the same observer with an interval of at least 1 month. For inter-observer variability, a second observer, blinded to the results of the first observer, independently performed the analysis. Reliability was evaluated using the intraclass correlation coefficient.

**Supplemental Table 1 Detailed CMR scan acquisition parameters of three 3.0T MR scanners**

|                                        | GE      |         | Siemens |         | Philips |         |
|----------------------------------------|---------|---------|---------|---------|---------|---------|
|                                        | Cine    | LGE     | Cine    | LGE     | Cine    | LGE     |
| TR (ms)                                | 3.6     | 6.2     | 3.1     | 4.1     | 3       | 6.1     |
| TE (ms)                                | 1.4     | 2.9     | 1.3     | 1.6     | 1.5     | 3       |
| FA (°)                                 | 60      | 25      | 45      | 20      | 45      | 25      |
| Receiver bandwidth (Hz/px)             | 1041.7  | 284.1   | 704     | 156     | 1268.9  | 147     |
| GRAPPA                                 | 2       | 2       | 2       | 2       | 2       | 2       |
| Acceleration factor                    |         |         |         |         |         |         |
| FOV (mm <sup>2</sup> )                 | 380*380 | 380*380 | 276*340 | 350*284 | 270*270 | 350*350 |
| In-plane resolution (mm <sup>2</sup> ) | 2.0*1.7 | 1.7*2.0 | 1.8*1.4 | 1.9*1.4 | 1.8*1.8 | 1.6*1.9 |
| Temporal resolution (ms)               | 86      | 149     | 40-50   | 140-150 | 50      | 154     |

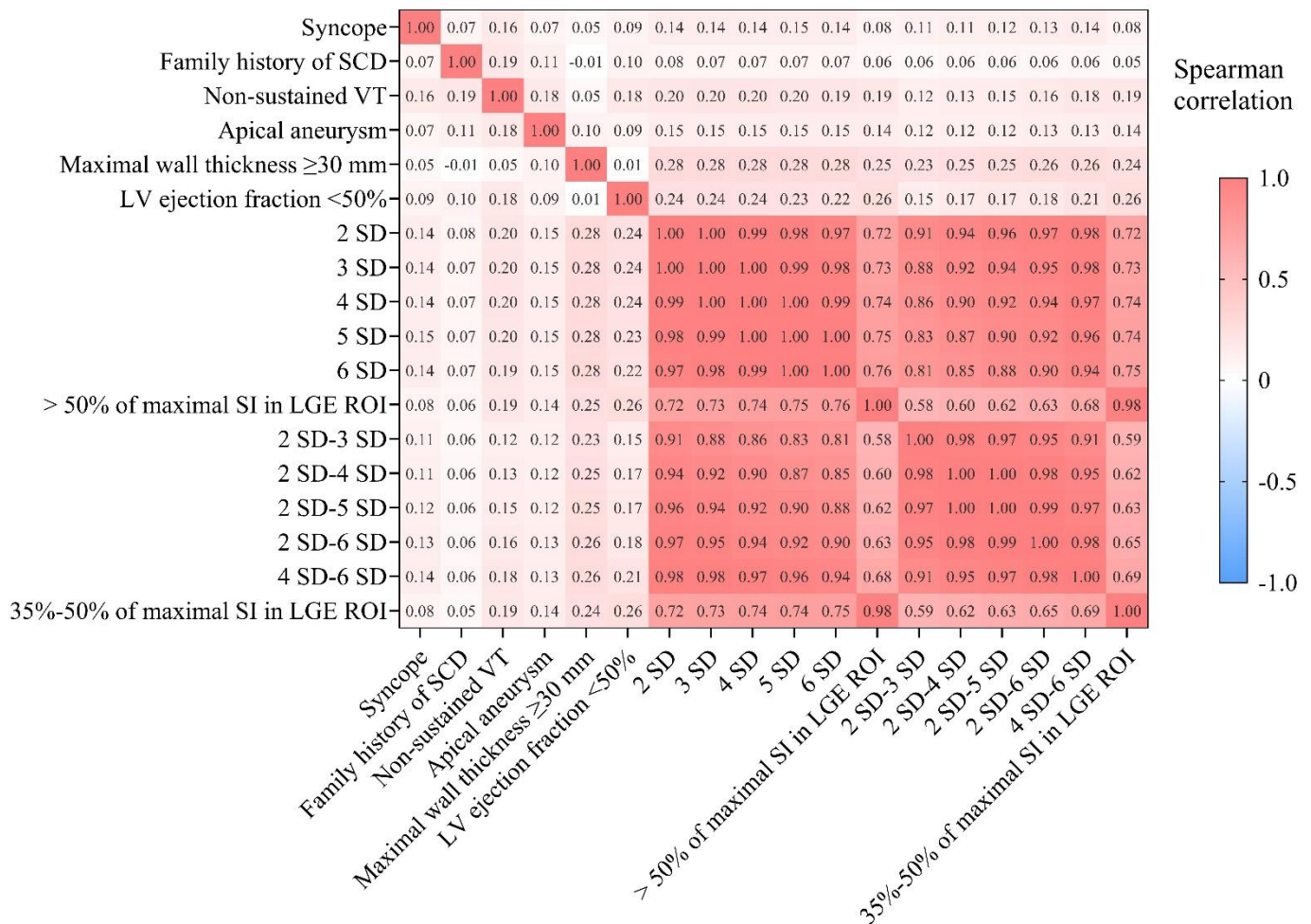
Cine images include 2-chamber, 3-chamber, 4-chamber views at long-axis and short-axis images. GE refers Discovery MR750 3.0T, GE Medical Systems, Milwaukee, USA; Siemens refers MAGNETOM Verio 3.0T, Siemens Healthineers, Erlangen, Germany; Phillips refers to Ingenia 3.0T, Phillips, Best, Netherlands. CMR, cardiovascular magnetic resonance; MR, magnetic resonance; LGE, late gadolinium enhancement; TR, repetition time; TE, echo time; FA, flip angel; FOV, field of view.

**Supplemental Table 2 Univariate Cox regression analysis for clinical and CMR variables and different LGE quantification methods in predicting SCD**

|                                             | HR (95% CI)         | P Value |
|---------------------------------------------|---------------------|---------|
| <b>Clinical variables</b>                   |                     |         |
| Age (years)                                 | 0.98 (0.95-1.01)    | 0.15    |
| Male sex                                    | 0.53 (0.24-1.18)    | 0.12    |
| Syncope                                     | 4.86 (2.08-11.36)   | <0.001  |
| Family history of SCD                       | 5.09 (1.74-14.90)   | 0.003   |
| Non-sustained VT                            | 23.29 (10.29-52.70) | <0.001  |
| NYHA class III/IV                           | 3.80 (1.50-9.64)    | 0.005   |
| Atrial fibrillation                         | 3.82 (1.65-8.87)    | 0.002   |
| <b>CMR variables</b>                        |                     |         |
| LA maximum volume (mL)                      | 1.00 (0.99-1.01)    | 0.66    |
| LV end-diastolic diameter (mm)              | 0.99 (0.93-1.05)    | 0.66    |
| LV maximal wall thickness (mm)              | 1.08 (1.05-1.12)    | <0.001  |
| LV maximal wall thickness $\geq 30$ mm      | 3.83 (1.31-11.25)   | 0.01    |
| LV mass index (g/m <sup>2</sup> )           | 1.02 (1.01-1.03)    | 0.001   |
| LV EDV index (mL/m <sup>2</sup> )           | 1.01 (0.99-1.03)    | 0.25    |
| Cardiac index (L/min/m <sup>2</sup> )       | 0.74 (0.46-1.17)    | 0.19    |
| LV ejection fraction (%)                    | 0.95 (0.93-0.98)    | <0.001  |
| LV ejection fraction <50%                   | 6.25 (2.77-14.07)   | <0.001  |
| LVOT obstruction                            | 1.24 (0.55-2.79)    | 0.61    |
| Apical aneurysm                             | 6.48 (2.77-15.17)   | <0.001  |
| <b>Different LGE quantification methods</b> |                     |         |
| 2 SD                                        | 1.07 (1.05-1.09)    | <0.001  |
| 3 SD                                        | 1.09 (1.05-1.09)    | <0.001  |
| 4 SD                                        | 1.07 (1.05-1.09)    | <0.001  |
| 5 SD                                        | 1.07 (1.05-1.09)    | <0.001  |
| 6 SD                                        | 1.07 (1.05-1.09)    | <0.001  |
| > 50% of MSI in LGE ROI                     | 1.10 (1.07-1.13)    | <0.001  |
| 2 SD-3 SD                                   | 1.28 (1.16-1.42)    | <0.001  |
| 2 SD-4 SD                                   | 1.18 (1.11-1.25)    | <0.001  |
| 2 SD-5 SD                                   | 1.15 (1.09-1.20)    | <0.001  |
| 2 SD-6 SD                                   | 1.13 (1.09-1.17)    | <0.001  |
| 4 SD-6 SD                                   | 1.32 (1.22-1.42)    | <0.001  |
| 35%-50% of MSI in LGE ROI                   | 1.22 (1.17-1.28)    | <0.001  |

CMR, cardiac magnetic resonance; LGE, late gadolinium enhancement; SCD, sudden cardiac death; HR, hazard ratio; CI, confidence interval; VT, ventricular tachycardia; NYHA, New York Heart Association; LA, left atrial; LV, left ventricular; EDV, end-diastolic volume; LVOT, left ventricular outflow tract; SD, standard deviation; MSI, maximum pixel signal intensity; ROI, region of interest.

**Figure S1 Associations between different extents of LGE and AHA/ACC risk markers for SCD**



LGE: late gadolinium enhancement; AHA, American Heart Association; ACC, American College of Cardiology; SCD, sudden cardiac death; VT, ventricular tachycardia; LV, left ventricular; SD, standard deviation; MSI, maximum pixel signal intensity; ROI, region of interest.