EDITORIAL COMMENT

LV Entropy by Native T1 Mapping in Patients With Hypertrophic Cardiomyopathy*

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Hypertrophic cardiomyopathy (HCM) is the most prevalent autosomal dominant genetic disease in the adult population.[1-3] Even though there are around two-thirds of patients with HCM experiencing a normal life span without significant morbidity,[4-6] the devastating events of ventricular arrhythmias (VAs) and sudden cardiac death (SCD) can occur in patients with identified high-risk features, and implantable cardioverter-defibrillator is indicated for lifesaving.[7] There are 2 practical risk stratification models proposed by the American College of Cardiology/American Heart Association (ACC/AHA)[8] and the European Society of Cardiology (ESC).[9,10] In summary, HCM patients with characteristics of severe left ventricular (LV) hypertrophy, LV outflow tract obstruction, LV systolic dysfunction, LV apical aneurysm, extensive late gadolinium enhancement (LGE), unexplained syncope, or a family history of sudden death are associated with VAs and SCD. Nevertheless, performance of the current risk scoring systems is not perfect. Validation from a recent large Mediterranean HCM cohort[11] demonstrated a high sensitivity of 96% but a modest specificity of 59% when applying the ACC/AHA scoring system; when using the ESC risk prediction model, it held a high specificity of 95%, but a relative low sensitivity (32%) in HCM patients with predictive risk for SCD ≥6%. Hence, the refinement of risk stratification in patients with HCM is the perpetual mission for clinicians.

Entropy, a novel measurement of myocardial tissue heterogeneity, has been explored to have predictive value of VAs and SCD in patients with various cardiomyopathies.[12-14] This emerging radiomics was estimated from LV LGE on cardiovascular cardiac magnetic resonance (CMR) with incremental value to the burden of LGE for risk stratification in the latest HCM studies.[15,16] Zhao et al[15] demonstrated that higher LGE entropy with a cutoff value ≥5.87 or ≥ third tertile (5.54) is associated with arrhythmic events in patients with HCM. In receiver-operating characteristic analysis, the area under the curve (AUC) of LV LGE entropy was 0.89, whereas the AUC was only 0.72 applying the ACC/AHA risk scoring system. Ye et al[16] investigated 68 HCM patients, and 31 patients had VAs. When adding LV LGE entropy to the burden of LGE, the AUC increased from 0.82 to 0.90 in the prediction of VAs. Recently, myomapping, the innovative technology in CMR, has been developed to identify pathologic processes of myocardium without the use of gadolinium.[17] By leveraging intrinsic tissue contrast through the native T1 tissue relaxation time, it can detect myocardial damage early and distinguish genotype-positive, phenotype-negative HCM patients from those with hypertensive heart disease.[18] Furthermore, a prolonged myocardial native T1 value in patients with HCM was associated with LV hypertrophy, and it suggested diffuse myocardial fibrosis, even in the absence of apparent LGE and hemodynamic obstruction.[19] Moreover, Thompson et al[20] discovered that native T1 and T1ρ values were elevated in HCM patients compared to healthy controls regardless of LGE status. The integration of native T1 mapping on CMR enables the detection of petty myocardial injury in patients with HCM without obvious LGE.

In this issue of *JACC: Asia*, Wang et al[21] reported on a prospective cohort study of 748 HCM patients with a

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median follow-up duration of 43 months. Forty (5.3%) patients had experienced SCD-related events, and 65 (8.7%) patients experienced composite cardiovascular death (CVD). Of note, Wang et al[21] estimated LV entropy from native T1 mapping instead of LGE images. Patients with an increased LV entropy cutoff value ≥5.86 derived from native T1 mapping were associated with a higher risk of SCD and composite CVD, even in those with low LGE burden <10%. Remarkably, the significant cutoff value of LV entropy estimated by native T1 mapping was similar to that estimated by LGE images in the previous study.[15] Moreover, the integration of T1 mapping-derived LV entropy and the ESC risk prediction model could provide an incremental prognostic value in patients with high (>10%) LGE burden with a C-index from 0.726 to 0.761 and 0.732 to 0.802 for SCD and CVD, respectively.

There are some issues in this study that warrant attention. First, unlike the generalizability of LGE images, there are several methods to generate T1 mapping,[22] and the native T1 value varies from different magnetic field intensity and various brands of CMR scanners.[23] Although LV entropy evaluates the tissue heterogeneity rather than the bare mean T1 value, the reproducibility of the prognostic value of T1 mapping-derived LV entropy needs further validation. Second, LGE entropy was estimated by a whole stack of LV LGE images in previous studies, whereas T1 entropy was generated by only 3 representative slices at the LV base, mid, and apex in the current study. Skipping diseased myocardium during image acquisition and the underestimation of T1 entropy is possible. Multicenter studies are warranted to validate the generalizability of current findings.

In summary, Wang et al[21] discovered the LV entropy derived from native T1 mapping is valuable for the identification of high-risk patients with HCM.[21] The adaptation of this novel radiomics may further refine the current risk stratification models in patients with HCM.

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