P5269

The impact of sarcomeric mutations on myocardial fibrosis and ventricular diastolic function in hypertrophic cardiomyopathy (SADS-TW HCM registry study)

C.-Y. Chen, L.-Y. Lin, Y.-H. Lin, Y.-C. Wang, J.-K. Lee, C.-K. Wu, L.-C. Lin, W.-J. Chen, P.-C. Lin, L.-T. Ho, Y.-B. Liu, L.-P. Lai, J.-J. Hwang, J.-M. Juang

National Taiwan University Hospital, Department of Internal Medicine, Taipei, Taiwan
On behalf of SADS-TW HCM registry
Funding Acknowledgement: None

Background: Hypertrophic cardiomyopathy (HCM) may manifest as diastolic dysfunction. The degree of myocardial fibrosis quantified by late gadolinium enhancement (LGE) in cardiac magnetic resonance (CMR) imaging is positively correlated with the risk of sudden cardiac death, whereas the impact of sarcomeric mutations on the ventricular diastolic function and myocardial fibrosis is unclear.
Purpose: We aimed to investigate the difference of the ventricular diastolic function and the degree of myocardial fibrosis between the HCM patients with and without sarcomeric mutation.
Methods: From 2014 to 2018, we prospectively enrolled 55 unrelated patients with HCM as defined by the 2014 European Society of Cardiology guideline. All enrolled patients underwent next-generation sequencing screening of 20 sarcomeric genes and CMR examination for the evaluation of left ventricular (LV) function, mass and LGE.
Results: After comparing the results with several public databases (Taiwan Biobank, gnomAD, HGMD, ClinVar) and performing in silico analyses (SIFT, Polyphen-2, PROVEAN, REVEL, CADD), 24 pathogenic variants were identified in 22 HCM patients. Although there were no differences in demographic data and clinical presentations between the mutation-positive and mutation-negative groups, the degree of LGE (14.2±14.3 vs 6.2±8.9%, p=0.015) and left atrial diameter (4.54±0.63 vs 4.00±0.49 cm, p<0.001) were significantly higher in the mutation-positive group, whereas the LV ejection fraction, mass, strain rates, peak ejection and filling rates, peak intra-LV and tricuspid regurgitation pressure gradient were similar in both groups.
Conclusions: The HCM patients with sarcomeric mutations had a higher degree of LV myocardial fibrosis than patients without mutations, which may imply that these mutations accelerate myocardial fibrosis in HCM. Nonetheless, there was no difference in diastolic function between the patients with and without sarcomeric mutation.

Table 1. Comparisons of the CMR parameters of HCM patients with and without sarcomeric mutation

	Sarcomeric mutation (+, M+), n=21	Sarcomeric mutation (–, M–), n=34	Control (C), n=36	M+ vs M– P-value	M+ vs C P-value	M– vs C P-value
PER/LVEDV, L/s	–4.73±1.18	–5.03±1.19	–3.49±0.78	0.361	<0.001*	<0.001*
PFR/LVEDV, L/s	4.05±1.00	3.74±1.25	5.52±1.20	0.341	<0.001*	<0.001*
Global radial diastolic strain rate, /s	–2.49±0.99	–2.74±1.51	–2.68±0.88	0.527	0.210	0.846
Global circumferential diastolic strain rate, /s	0.89±0.19	0.92±0.30	1.49±0.32	0.684	<0.001*	<0.001*
Global longitudinal diastolic strain rate, /s	0.64±0.19	0.62±0.24	0.95±0.27	0.744	<0.001*	<0.001*

C: control; LVEDV: left ventricular end-diastolic volume; M+: sarcomeric mutation (+); M–: sarcomeric mutation (–); PER: peak ejection rate; PFR: peak filling rate.
*p<0.05.