Abstract: **P6164**

A founder mutation of the myosin binding protein-C gene in hypertrophic cardiomyopathy and adverse outcomes with compound heterozygosity

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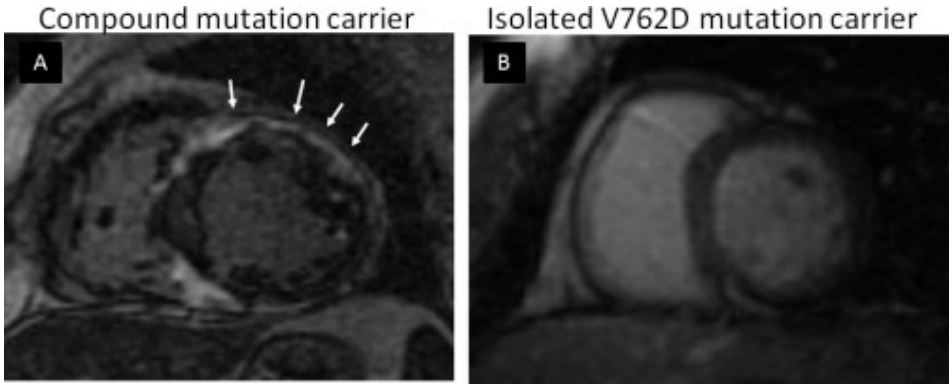
Purpose: Hypertrophic cardiomyopathy (HCM) is the most common genetic heart disease, caused by sarcomeric genes mutations. Although most of founder mutation carriers that arose from a common ancestor exhibit favorable clinical phenotypes, there still remain small fractions of these carriers associated with increased cardiovascular events. However, few data exist regarding defining factors that modify phenotypes of these patients particularly in terms of multiple gene mutations. Therefore, we assessed genotype-phenotype correlations and investigated factors that contribute to phenotypic diversities of the founder mutation carriers.

Methods and results: We screened unrelated 488 probands with HCM for sarcomeric genes mutations. We identified a prevalent founder mutation (V762D) in the MYBPC3 in 33 subjects from 19 families. Among them, 28 carriers harbored isolated V762D mutation and exhibited a late onset of overt HCM than other MYBPC3 mutations carriers (62.8±3.0 years vs 50.1±2.6 years, $p<0.05$). In contrast, remaining 5 carriers had additional sarcomere-genes mutations (3 in the MYBPC3, 2 in the cardiac troponin T gene) and showed unfavorable phenotypes such as early disease onset and massive left ventricular fibrosis (Figure) determined by the late gadolinium enhancement of cardiac magnetic imaging.

Conclusion: Mutation carriers with founder MYBPC3 V762D can develop unfavorable phenotypes of HCM when combined with other sarcomere gene mutations.



Cardiac magnetic resonance images.