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LETTER TO THE EDITOR

Response by Sakamoto et al to Letter Regarding Article, "Left-Dominant Arrhythmogenic Cardiomyopathy With Heterozygous Mutations in *DSP* and *MYBPC3*"

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In Response:

We wish to thank Dr Pérez-Riera et al for their interest in our article[1] and for their thoughtful comments. They rightly point out that 4 additional 12-lead ECG features in Figure are relevant to the ECG characteristics of left-dominant arrhythmogenic cardiomyopathy.

Cardiac computed tomography revealed low-attenuation areas and magnetic resonance imaging showed late gadolinium enhancement areas on the mid myocardial septum and subepicardial anterior-lateral left ventricular myocardium, consistent with fibrofatty infiltration. We agree with their opinion because the characteristic ECG features and origin of the premature ventricular complexes correspond to the distribution of fibrofatty infiltration, including the subepicardial lateral lesion.

A genetic analysis revealed heterozygous pathogenic mutations in the *DSP* (desmoplakin gene) and *MYBPC3* (myosin-binding protein C gene). Recently, variable clinical expressions of both arrhythmogenic cardiomyopathy and hypertrophic cardiomyopathy have been reported in members of an Italian family who carried heterozygous mutations in *DSP* and *MYBPC3*.[2] Among the 4 clinically evaluated double heterozygotes for the mutations in *DSP* and *MYBPC3*, 2 were diagnosed with arrhythmogenic cardiomyopathy and 2 with hypertrophic cardiomyopathy.

In our case, the clinical phenotype was left-dominant arrhythmogenic cardiomyopathy, but the histological findings from the endomyocardial biopsy showed unique features. The histological findings suggested that the fibrofatty replacement and intercalated disc remodeling were associated with the *DSP* mutation. The findings also suggested that the hypertrophy and disarrangement of the myocytes were associated with the *MYBPC3* mutation. The combined effects of the 2 gene mutations possibly represent a novel pathophysiological mechanism of left-dominant arrhythmogenic cardiomyopathy.

ARTICLE INFORMATION

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Disclosures

None.

REFERENCES

1. Sakamoto N, Natori S, Hosoguchi S, Minoshima A, Noro T, Akasaka K, Sato N, Ohno S, Ikeda Y, Ishibashi-Ueda H, Horie M, Hasebe N. Left-dominant arrhythmogenic cardiomyopathy with heterozygous mutations in DSP and MYBPC3. *Circ Cardiovasc Imaging*. 2019;12:e008913. doi: 10.1161/CIRCIMAGING.119.008913
2. De Bortoli M, Calore C, Lorenzon A, Calore M, Poloni G, Mazzotti E, Rigato I, Marra MP, Melacini P, Iliceto S, Thiene G, Basso C, Daliento L, Corrado D, Rampazzo A, Bauce B. Co-inheritance of mutations associated with arrhythmogenic cardiomyopathy and hypertrophic cardiomyopathy. *Eur J Hum Genet*. 2017;25:1165–1169. doi: 10.1038/ejhg.2017.109