# Clinical features of Brugada syndrome patients with SCN5A variants

Shou Okamura[1], Hidenori Ochi[1], Mika Nakashima[1], Rie Akiyama[1], Takehito Tokuyama[1], Yousaku Okubo[1], Shunsuke Miyauchi[1], Shogo Miyamoto[1], Naoto Oguri[1], Yukimi Uotani[1], Takumi Sakai[1], Motoki Furutani[1], Yasuki Kihara[2], and Yukiko Nakano[1]

[1]Hiroshima Daigaku Daigakuin Ikei Kagaku Kenkyuka
[2]Kobe Shiritsu Iryo Center Chuo Shimin Byoin

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## Abstract

**Background** *SCN5A* is the most common susceptibility gene in patients with Brugada syndrome (BrS); however, the interpretation and management of benign or variants of unknown clinical significance (VUS) in *SCN5A* remains a challenge despite the availability of genetic testing. **Objective** This study aimed to investigate the relationship between the *SCN5A* variants and clinical symptoms of BrS patients. **Methods** We resequenced the *SCN5A* gene in 239 patients diagnosed with BrS at Hiroshima University Hospital and analyzed the association between the *SCN5A* variants and clinical features, 12-lead electrocardiography (ECG) parameters, or signal-averaged ECG. **Results** Overall, 84 *SCN5A* variants were identified: 55 benign, 7 pathogenic, and 22 VUS . No significant difference in the incidence of previous cardiac events was observed between patients with and without *SCA5A* benign variants. The female proportion was higher in BrS patients with *SCN5A* VUS or pathogenic variants. Moreover, the symptomatic proportion was higher in BrS patients with *SCN5A* VUS or pathogenic variants. Multivariate analyses revealed that the presence of *SCN5A* VUS or pathogenic variants, longer r-J interval in lead V1, and the presence of fragmented QRS were independently associated with the cardiac events in BrS patients and that positive late potentials, longer LAS40, and lower RMS40 were significantly associated with symptomatic BrS in patients carrying *SCN5A* VUS. **Conclusions** The *SCN5A* VUS or pathogenic variants were found to be independent risk factors for the cardiac events in the BrS patients. In BrS patients with *SCN5A* VUS, the signal-averaged ECG was the key to risk stratification for cardiac events.

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