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## The Theory of Relativity in E (ectopy) and C (coupling): Who Will Prove It?

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Ventricular premature complexes (VPCs) are commonly observed arrhythmias in healthy individuals. It is well-known that frequent VPCs can lead to left ventricular dilatation and systolic dysfunction, termed VPC-mediated cardiomyopathy.<sup>1)</sup> Based on many studies that aimed to reveal the characteristics of VPCs that have an influence on hemodynamics, site of origin, coupling interval (Cl), and VPC burden have been chosen as the most promising leads; however, there are no definite answers, and many controversies still remain. There are no firm guidelines to assist physicians in treating patients with frequent VPCs.

Yokokawa et al.<sup>2)</sup> showed that the absence of symptoms is independently associated with VPC-induced cardiomyopathy. Park et al.<sup>3)</sup> discussed that the absence of typical VPC-related symptoms may be a risk factor for cardiomyopathy and be associated with adverse outcomes. This may be because asymptomatic patients visit the clinic at later stages than do patients with symptoms. Other studies have shown that patients with VPC-mediated cardiomyopathy have a significantly longer duration of symptoms compared with patients without cardiomyopathy.<sup>2)</sup> This suggests

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that frequent VPCs over a long period of years, rather than months, may be required to result in cardiomyopathy. We could speculate that asymptomatic patients are diagnosed later, thus resulting in higher risk of cardiomyopathy, but the question still remains of why patients with the same VPC burden differ in symptoms.

Park et al.<sup>4)</sup> prospectively enrolled 109 patients (30 asymptomatic and 79 symptomatic) with idiopathic outflow-tract-origin VPCs and attempted to identify the electrocardiographic components related to typical VPC symptoms such as palpitations or "dropped beats." The study provides us with new insights in that the results show that VPC-related symptoms were associated with the VPC:Cl ratio (VPC Cl/sinus cycle length×100%), that is, Cl adjusted by sinus rate.

Although CI is the most important factor in determining VPCrelated symptoms, the clinical implications are not well explained in the study by Park et al.<sup>4)</sup> Thanavaro et al.<sup>5)</sup> reported that when CI is below 400 ms or above 600 ms, ventricular couplets or runs seem to be more frequent. An animal study that used 12 canines showed that the hemodynamic changes during a VPC are closely related to the site of origin and the Cl.<sup>6)</sup> Sun et al.<sup>7)</sup> reported that frequent VPCs with short CIs were related to markedly reduced cardiac output and low ejection fractions in asymptomatic children. Del Carpio Munoz et al.<sup>8)</sup> meanwhile, reported that there was no association between VPC-related cardiomyopathy and CI.

There were limitations in the Park et al. study<sup>4)</sup> that the authors did note, such as the enrollment of more symptomatic than asymptomatic patients and variations in patient symptoms and sinus cycle length. The most important limitation is that the enrolled patients did not represent the general VPC population. Because the indications of radiofrequency catheter ablation for asymptomatic patients (13 of 30 patients) were mostly different from those for patients with symptoms, patients with implantable cardioverter defibrillators or those with low ejection fractions were enrolled in the study. These patients do not represent the asymptomatic, frequent-VPC patients whom we encounter and agonize over treating in our outpatient clinics. In addition, there was a difference

in medication history between the two groups. The asymptomatic group had more patients with slower heart rates and more patients on antiarrhythmic treatment, which could have been the reason for the lack of symptoms or electrocardiography (ECG) interval changes.

Although it is unfortunate that this study did not establish a firm relationship between VPC-related symptoms and ECG parameters or its influence on VPC-related cardiomyopathy, we anticipate further work on the basis of the study. In addition, by suggesting that there is a difference in the hemodynamics of symptomatic and asymptomatic VPC patients, this study will be valuable in treating and studying asymptomatic VPC patients.

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