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Original Article

# Spatial and transmural repolarization, and dispersion of repolarization and late potentials evaluated using signal-averaged vector-projected 187-channel high-resolution electrocardiogram in Brugada syndrome

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ABSTRACT

*Background:* Vector-projected 187-channel electrocardiograms (ECGs) were recorded in 45 patients with a Brugada-type ECG to evaluate spatial and transmural repolarization and dispersion of action potential duration in Brugada syndrome (BS).
*Methods:* Corrected recovery time (RT-c, R wave peak to the first positive maximum derivative of the T wave with Bazett correction) and RT-c dispersion were calculated. The corrected T peak-end interval (T(p-e)-c, T wave peak to the end of the T wave with Bazett correction) and T(p-e)-c dispersion were calculated.
*Results:* RT-c dispersion and T(p-e)-c interval were longer in patients with a type 1 ECG, but there was no significant difference in Tp-e dispersion between patients with a type 1 and those with a type 2/3 ECG. No significant correlation was noted between RT-c dispersion, T(p-e)-c dispersion, and symptoms. Late potentials ($P=0.023$) and a family history of sudden cardiac death ($P=0.0017$) were correlated with symptoms.
*Conclusions:* Spatial dispersion of repolarization may constitute the electrocardiographic pattern of the Brugada type ECG and conduction disturbance in addition to repolarization abnormality may contribute to the development of malignant ventricular tachyarrhythmias.


## 1. Introduction

Brugada syndrome (BS) is an arrhythmogenic entity characterized by the presence of ST-segment elevation in leads V1–V3 on surface electrocardiogram (ECG), the absence of structural heart disease, and a high risk of ventricular tachycardia/ventricular fibrillation (VT/VF) and sudden cardiac death (SCD) [1–3]. Risk stratification is controversial, especially in asymptomatic individuals [4–6]. Transmural dispersion of repolarization within the ventricular myocardium has been suggested to underlie arrhythmogenesis in BS [7], and ECG markers of ventricular repolarization have been reported for the identification of high-risk patients with BS [8]. We investigated whether ECG-based spatial and transmural ventricular depolarization and repolarization values are potential risk factors for arrhythmic events in BS patients. In the present study, we used the recently developed signal-averaged vector-projected 187-channel high-resolution ECG (187-channel SAVP-ECG).

## 2. Methods

### 2.1. Study patients

The study group comprised 45 consecutive patients (male/female ratio: 43/2; mean age, 51.5 ± 14.4 years) with spontaneous ($n=26$) or drug-induced (pilsicainide 1 mg/kg) ($n=19$) type 1 BS ECG phenotype. The ECG diagnosis of BS was based strictly on the recommendations of the Second Consensus Conference [3]. Structural heart disease was ruled out in all study patients by performing transthoracic echocardiography. Those with a history of syncope, documented sustained ventricular arrhythmia,

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or aborted SCD were considered symptomatic. The study was approved by the Institutional Review Committee of Nihon University Hospital, and the patients signed informed consent for 187-channel SAVP-ECG recording, mutation screening for the SCN5A gene, and invasive electrophysiological study.

### 2.2. 187-channel SAVP ECG

187-channel SAVP-ECGs were obtained with an electrode lead system, an input box, a high-precision amplifier (HRES-1000, Fukuda Denshi Co. Ltd., Tokyo, Japan), and a personal computer. The input box generated a modified *X*–*Y*–*Z*-lead ECG, and the vector-projected 187-channel synthesized ECGs via a Mason–Likar lead system. The input signal ( $\pm$550 mV) was digitized at 2 kHz by an analog-to-digital (A/D) converter with a resolution of 0.076 μV. Ten electrodes were attached to the right shoulder, left shoulder, left lower abdomen, right lower abdomen, and the usual V1–V6 recording sites. The 187-channel SAVP-ECG recording was performed with patients in a resting position. Details of the187-channel SAVP-ECG have been reported previously [9–11]. The 187-channel SAVP-ECG variables measured in the current study are described below.

### 2.3. Repolarization

The RT interval was defined as the time between the peak of the R wave and the maximum positive peak of the first derivative of the T wave, which was defined as the peak of the T wave. The RT end interval (RTend) was defined as the time between the peak of the R wave and the maximum negative derivative of the T wave. T peak-end (T(p-e)) was defined as the time between the T peak and the maximum negative derivative of the T wave (Fig. 1). RT dispersion was automatically calculated as the difference between the longest RT interval (RTmax) and the shortest RT interval (RTmin). RTend dispersion was automatically calculated as the difference between the longest RTend interval (RTend max) and the shortest RTend interval (RTend min). T peak-end dispersion was also automatically calculated as the difference between the longest T peak-end interval (Tp-e max) and the shortest T peak-end interval (Tp-e min). The corrected RT interval (RT-c), corrected RTend interval (RTend-c), and corrected T peak-end interval (T(p-e)-c) were calculated according to the Bazett formula. Average RT-c, average RTend-c, and average T(p-e)-c were calculated as the average value of each of these variables as detected on the 187-channel SAVP-ECG. Formulas for the variables are as follows:

Average RT-c = average of each RT-c
RT-c dispersion = RT-c max − RT-c min
Average RTend-c = average of each RTend-c
RTend-c dispersion = RTend-c max − RTend-c min
Average T(p-e)-c = average of each T(p-e)-c
T(p-e)-c dispersion = T(p-e)-c max − T(p-e)-c min
Average RT-c dispersion = average of (each RT-c − RT min-c)
Average RTend-c dispersion = average of (each RTend-c − RTend min-c)
Average T(p-e)-c dispersion = average of [each T(p-e)-c − T(p-e)-c min]

The RTc, RTe-c, and T(p-e)-c maps were displayed as 256-color coordinated maps according to the time difference. In brief, blue represents $<$ 40 ms; green-yellow, 40 − 79 ms; orange, 80 − 99 ms; and red $\geq$ 100 ms.

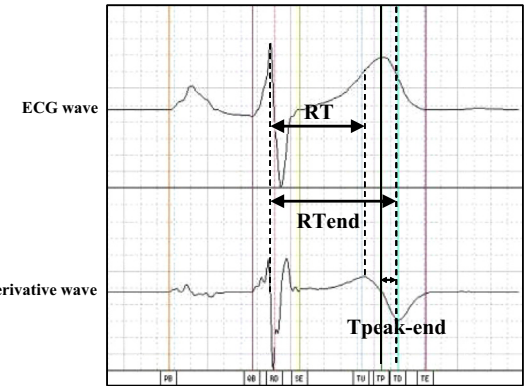


**Fig. 1.** Reference point for RT interval, T peak-end interval, and RTend interval. The RT interval was defined as the time between the peak point of the R wave and the positive maximum peak of the first derivative of the T wave. The T peak-end was defined as the time between the peak point of the T wave and the negative maximum peak of the first derivative of the T wave. RTend was defined as the time between the peak point of the R wave and the negative maximum peak of the first derivative of the T wave (modified from Nakai et al. [9]).

### 2.4. Depolarization

The modified *X*–*Y*–*Z*-lead ECG and the synthesized signals from the 187-channel SAVP-ECGs were amplified and passed through a finite impulse response (FIR) digital filter (frequency characterization: 27th order) with a low frequency of 45 Hz and a high frequency of 280 Hz, and then A/D converted with 12-bit accuracy at 2000 samples/s. After rejection of ectopic beats, ECG signals over 10 min were averaged by means of the signal-processing system. The non-filtered *X*–*Y*–*Z*-lead ECG, filtered *X*–*Y*–*Z*-lead ECG, and vector magnitude ECG were displayed on the same time scale (Fig. 1). The filtered QRS (fQRS) duration was determined automatically according to the beginning and end of the vector magnitude ECG by the points exceeding 5 times the noise levels. The root mean square of the last 40 ms ($RMS_{40}$) was measured by the integrated magnitude at 40 ms before the QRSend of the vector magnitude ECG. In addition, we measured the duration of low-amplitude signals $<$ 40 μV ($LAS_{40}$) on the vector magnitude ECG. Spatial distribution of integrated high-frequency late potentials (HFLPs), as shown by 187-channel SAVP-ECG mapping, was calculated as the integration of the electrical potentials of fQRS measured between 30 ms (initial offset) before the QRSend (QRSend-30) and the QRSend. The endpoint in each channel was defined as the endpoint of the QRS, where the average exceeded the mean plus 5 standard deviations of the noise sample. The integrated HFLP map based on the 187-channel SAVP-ECGs was defined graphically by the gray scale that exceeded 5 times the mean noise level. The spatial distribution of integrated HFLPs based on the 187-channel SAVP-ECGs was superimposed on the RTc and T(p-e)-c dispersion map (Fig. 2).

### 2.5. Electrophysiological study

A comprehensive electrophysiological study was performed in 27 patients in a fasting, drug-free, non-sedated state. For patients who underwent coronary artery stent implantation, programmed ventricular stimulation was performed at 1 month after stent implantation. After obtaining access to the right femoral vein at 4 sites, 1 quadripolar catheter (Biosense-Webster, Diamond Bar, CA, USA) was positioned at the right atrial appendage, 1 octapolar catheter (Biosense-Webster) was positioned at the his bundle electrogram recording site, and 2 steerable quadripolar catheters (6 F) with an interelectrode distance of 2–5–2 mm (Biosense-Webster) were positioned in the right ventricular apex and outflow tract. Endocardial potentials were filtered to recording frequencies of 30 − 500 Hz and recorded on a BARD computer system (BARD Lab Pro, BARD Electrophysiology, Lowell, MA, USA). Programmed electrical stimulation