Which number of morphological types of ventricular premature beats predicts poor prognosis in subjects with various cardiomyopathies without obstructed coronary arteries?

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Conduction abnormalities within the QRS complex manifest as fragmented QRS waves, which appear as multiple spikes within the QRS wave complex. Fragmented QRS waves are important markers for spontaneous ventricular fibrillation in Brugada syndrome and predict the occurrence of high risk syncope [1].

Ventricular premature beats (VPBs) of long duration (≥160 ms) with fragmented QRS waves are simple and reliable 12-lead electrocardiographic (ECG) markers for a dilated and globally hypokinetic left ventricle (LV) in a nonspecifically-diseased heart, while a VPB with smooth contour or narrow notching with short duration (<160 ms) reflects a normal-sized heart with normal or near-normal systolic function despite the presence of underlying disease [2].

Various morphologies of VPBs are observed in cardiomyopathy subjects especially in subjects with hypertrophic cardiomyopathy (HCM), but their significance is unknown.

In this study, we evaluated the significance of the numbers of morphological types of VPBs and VPBs with fragmented QRS waves (fragmented VPBs) on 12-lead Holter ECG in various cardiomyopathy subjects without obstructed coronary arteries as diagnosed by multislice computed tomography (CT).

This was a retrospective analysis of 64 consecutive subjects (46 males, mean age 61 ± 14 years) who satisfied the definitions of cardiomyopathies published in Circulation 2006 [3] and did not have any obstructed coronary arteries on CT. Final clinical diagnosis (N = 64) were represented in Table 1. Percentage of HCM was 75%. Patients' characteristics were represented in Table 2. They underwent cardiac multislice CT and 12-lead Holter ECG within 12 months of each other from July 2007 to April 2012. Exclusion criteria was as follows: coronary artery stenosis (>50%) on CT and previous myocardial infarction. Subjects were followed for a median of 50 months for occurrence of major adverse cardiovascular events (MACE). MACE included cardiovascular death, critical ventricular arrhythmia and hospitalization due to heart failure. Critical ventricular arrhythmias included subjects with appropriate implantable cardioverter defibrillator therapy such as appropriate discharge of implantable cardioverter defibrillator and anti-tachycardia pacing for ventricular tachycardia and performance of radiofrequency catheter ablation of ventricular arrhythmia.

A fragmented VPB was defined as a VPB with one or more notches in the R or S waves on a routine 12-lead Holter ECG [4,5] (Fig. 1). Obvious complete right or left bundle branch block-shaped VPBs were excluded from fragmented VPBs in this analysis. The numbers of morphological types of all VPBs and fragmented VPBs were counted automatically, but were manually revised by experienced technologists. Thereafter, an experienced cardiologist blinded to the CT findings confirmed the results of the printed results.

Retrospective ECG gated CT scans were performed on all subjects to evaluate coronary arteries, myocardium and cardiac function [6–9] depending upon the ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/SCAI/SCMR 2010 appropriate use criteria for cardiac CT [10].

The total numbers of morphological types of all VPBs and fragmented VPBs were 10.1 ± 21.6 and 2.8 ± 2.2, respectively. MACE occurred in a total of 9 subjects (14.1%) (7 males, mean age 50 ± 21 years) (cardiovascular death 1, critical ventricular arrhythmia 5, and hospitalization due to heart failure 3).

According to the receiver operating characteristic (ROC) curve analysis, the best cutoff value for the number of morphological types of all VPBs to distinguish between the subjects with and without MACE was 12 with sensitivity 66.7%, specificity 92.7% and are under the curve (AUC) 0.783 (Fig. 2). By Kaplan–Meier analysis, there was a significant difference in the occurrence of MACE between the subjects with morphological types of all VPBs ≥ 12 and < 12 ($P < 0.001$) during the follow-up period (Fig. 3).

According to another ROC curve analysis, the best cutoff value for the number of morphological types of fragmented VPBs to distinguish between the subjects with and without MACE was 2 with sensitivity 100%, specificity 41.8% and AUC 0.762 (Fig. 4). By Kaplan–Meier

Table 1
Final clinical diagnosis (N = 64) of the cardiomyopathy subjects without obstructed coronary arteries in this study.
Percentage of hypertrophic cardiomyopathy was 75%.

Hypertrophic cardiomyopathy	48 (75.0%)
Dilated cardiomyopathy	5 (7.8%)
Arrhythmogenic right ventricular cardiomyopathy	1 (1.6%)
Inflammatory cardiomyopathy	4 (6.3%)
Cardiac amyloidosis	1 (1.6%)
Left ventricular noncompaction	1 (1.6%)
Stress cardiomyopathy	1 (1.6%)
Unidentified cardiomyopathy	3 (4.7%)

Table 2
Patients' characteristics of the cardiomyopathy subjects without obstructed coronary arteries in this study.

All subjects (N = 64)	
Age (years)	61 ± 14
Male	46 (71.9%)
Hypertension	30 (46.9%)
Diabetes mellitus	9 (14.1%)
Hyperlipidemia	20 (31.3%)
Smoking	21 (32.8%)
Administration of angiotensin receptor blocker	27 (42.2%)
Administration of angiotensin converting enzyme inhibitor	3 (4.7%)
Administration of β blocker	45 (70.3%)
Administration of statin	17 (26.6%)
Follow-up period (months)	39.5 ± 24.2 (Median 50)

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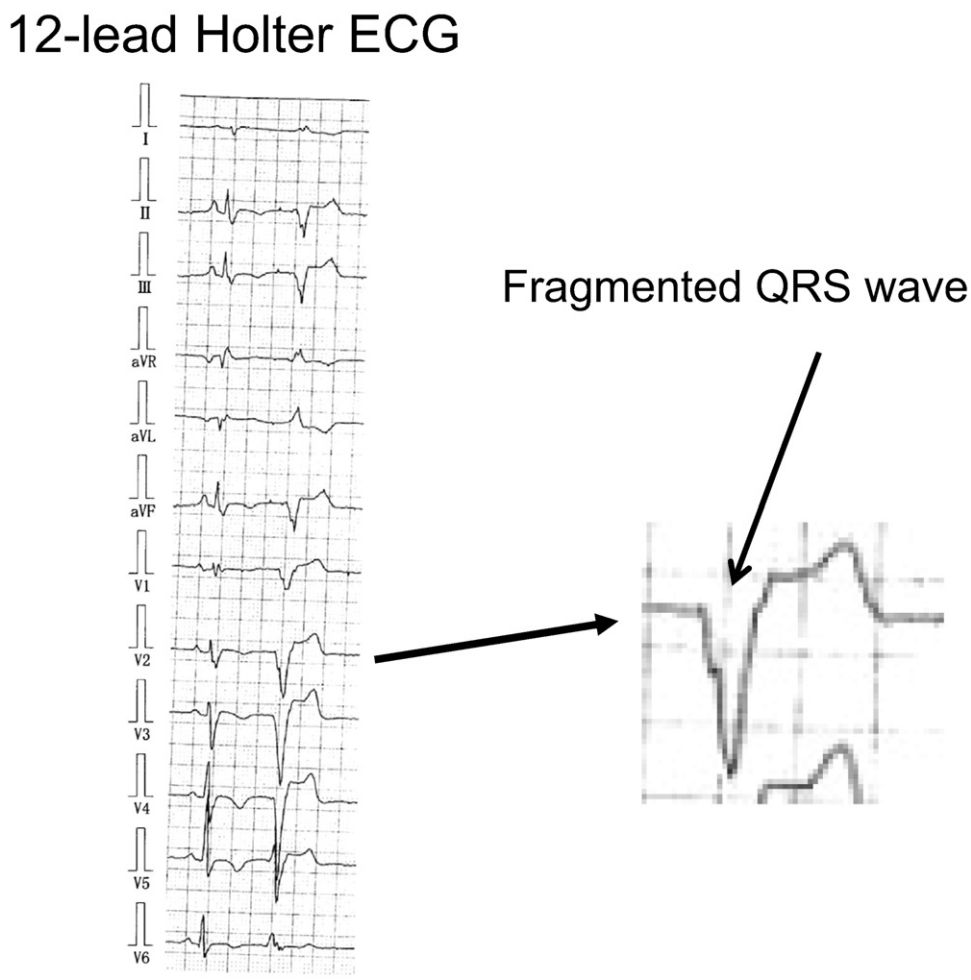

Fig. 1. Typical images of fragmented ventricular premature beats (VPBs) on V1 leads acquired from 12-lead Holter electrocardiogram.A fragmented VPB was defined as a VPB with one or more notches in the R or S waves on a routine 12-lead Holter electrocardiogram.

analysis, there was a significant difference in the occurrence of MACE between the subjects with morphological types of fragmented VPBs ≥ 2 and < 2 (P = 0.013) during the follow-up period (Fig. 5).

A the sub-analysis of this study, we also determined the significance of the number of morphological types of VPBs with fragmented QRS waves on 12-lead Holter ECG in only 48 HCM subjects (36 males; mean age 61 ± 13 years) without obstructed coronary arteries on multislice CT. Subjects were followed for a median of 51 months for occurrence of MACE.

Distribution of Maron HCM types in this study population was represented in Fig. 6. Patients' characteristics and sudden cardiac death risk factors for HCM [11] were represented in Tables 3 and 4.

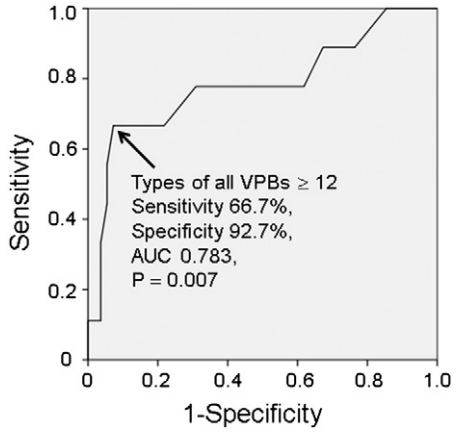

Fig. 2. Receiver operating characteristic (ROC) curve for major adverse cardiovascular events (MACE) in the cardiomyopathy subjects without obstructed coronary arteries using numbers of morphological types of all ventricular premature beats (VPBs).According to the ROC curve, the best cutoff value for the number of morphological types of all VPBs to distinguish between subjects with and without MACE was 12 with sensitivity 66.7%, specificity 92.7% and area under the curve (AUC) 0.783.

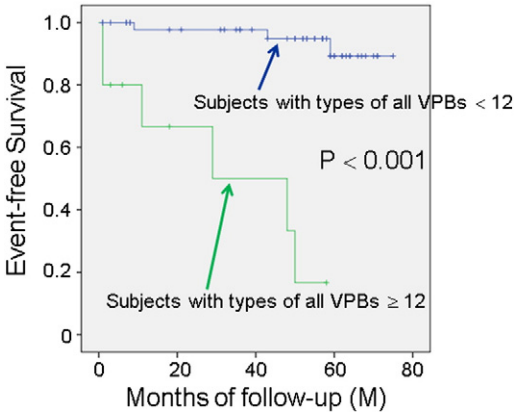

Fig. 3. Kaplan–Meier survival curve of the cardiomyopathy subjects without obstructed coronary arteries for major adverse cardiovascular events (MACE) using numbers of morphological types of all ventricular premature beats (VPBs).By Kaplan–Meier analysis, there was a significant difference in the occurrence of MACE between the subjects with morphological types of all VPBs ≥ 12 and < 12 (P < 0.001) during the follow-up period.