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Original article

# The Selvester QRS score as a predictor of cardiac events in nonischemic dilated cardiomyopathy

Hiroaki Hiraiwa (MD)[a], Takahiro Okumura (MD, PhD) [a,*], Akinori Sawamura (MD, PhD)[a], Yuki Sugiura (MD)[a], Toru Kondo (MD)[a], Naoki Watanabe (MD)[a], Soichiro Aoki (MD)[a], Takeo Ichii (MD)[a], Katsuhide Kitagawa (MD)[a], Naoaki Kano (MD)[a], Kenji Fukaya (MD, PhD)[a], Kenji Furusawa (MD)[a], Ryota Morimoto (MD, PhD)[a,b], Kyosuke Takeshita (MD, PhD)[a,c], Yasuko K. Bando (MD, PhD)[a], Toyoaki Murohara (MD, PhD, FJCC)[a]

[a] Department of Cardiology, Nagoya University Graduate School of Medicine, Nagoya, Japan
[b] Department of CKD Initiatives Internal Medicine, Nagoya University Graduate School of Medicine, Nagoya, Japan
[c] Department of Clinical Laboratory, Nagoya University Hospital, Nagoya, Japan

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ABSTRACT

*Background:* Myocardial fibrosis is associated with poor prognosis in nonischemic dilated cardiomyopathy (NIDCM) patients. The Selvester QRS score on 12-lead electrocardiogram is associated with both the amount of myocardial scar and poor prognosis in myocardial infarction patients. However, its use in NIDCM patients is limited. We investigated the prognostic value of the QRS score and its association with collagen volume fraction (CVF) in NIDCM patients.

*Methods:* We enrolled 91 consecutive NIDCM patients (66 men, 53 ± 13 years) without permanent pacemakers or cardiac resynchronization therapy devices. The Selvester QRS score was calculated by two expert cardiologists at NIDCM diagnosis. All patients were followed up over 4.5 ± 3.2 years. Cardiac events were defined as a composite of cardiac death, hospitalization for worsening heart failure, and lethal arrhythmia. We also evaluated CVF using endomyocardial biopsy samples.

*Results:* At baseline, the left ventricular ejection fraction was 32 ± 9%, plasma brain natriuretic peptide level was 80 [43–237] pg/mL, and mean Selvester QRS score was 4.1 points. Twenty cardiac events were observed (cardiac death, $n = 1$; hospitalization for worsening heart failure, $n = 16$; lethal arrhythmia, $n = 3$). Cox proportional hazard regression analysis revealed that the Selvester QRS score was an independent determinant of cardiac events (hazard ratio, 1.32; 95% confidence interval, 1.05–1.67; $p = 0.02$). The best cut-off value was determined as 3 points, with 85% sensitivity and 47% specificity (area under the curve, 0.688, $p = 0.011$). In Kaplan–Meier survival analysis, the QRS score ≥3 group had more cardiac events than the QRS score <3 group (log-rank, $p = 0.007$). Further, there was a significant positive correlation of Selvester QRS score with CVF ($r = 0.46$, $p < 0.001$).

*Conclusions:* The Selvester QRS score can predict future cardiac events in NIDCM, reflecting myocardial fibrosis assessed by CVF.



## Introduction

Heart failure (HF) is a progressive systemic disease and a major public health problem with economic and social burden in developed countries. Despite modern progress in medical management, HF remains a common cause of recurrent hospitalization or death [1]. A number of prognostic predictors of HF have been reported, including plasma brain natriuretic peptide (BNP) level on blood test, cholesterol metabolism, circadian blood pressure profile, and peak oxygen consumption on cardiopulmonary exercise testing [2–7]. In particular, the progression of myocardial fibrosis assessed by late gadolinium enhancement on cardiovascular magnetic resonance (CMR) or endomyocardial biopsy (EMB) is associated with poor outcome in nonischemic dilated cardiomyopathy (NIDCM) [8]. However, development of a

* Corresponding author at: Department of Cardiology, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466-8550, Japan.
*E-mail address:* takaoku@med.nagoya-u.ac.jp (T. Okumura).

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simple, low cost, and noninvasive method for risk stratification is urgently required to reduce healthcare costs and to reduce the burden of HF for patients and medical staff.

Twelve-lead electrocardiogram (ECG) is a standard cardiac examination, and is low cost, noninvasive, reproducible, rapid, and usable anywhere. Abnormal findings on ECG such as fragmented QRS or bundle branch block [9–11] and prolonged QRS duration were reported as prognostic predictors in HF patients [12,13]. In the 1980s, Selvester et al. developed a unique QRS scoring system composed of 32 points, in which each point was allocated 3% of the left ventricular (LV) mass [14]. In addition, the QRS score was reported to reflect and quantify myocardial scar volume despite the presence of abnormal ventricular conduction, and to have prognostic value in patients with ischemic cardiomyopathy [15–17]. However, the prognostic value of the QRS score in NIDCM patients remains unclear.

In the present study, we hypothesized that the Selvester QRS score predicts future cardiac events in NIDCM patients, reflecting the amount of myocardial fibrosis. The aim of this study was to investigate the prognostic value of the Selvester QRS score and the relationship between the QRS score and myocardial fibrosis in NIDCM.

## Methods

### *Study population*

We enrolled 91consecutive NIDCM patients between April 2006 and March 2015 in this single center prospective observational study. All patients were hospitalized in our institute for making a definite diagnosis of cardiomyopathies under each individual stable condition of HF. The patients underwent 12-lead ECG, laboratory measurements, echocardiography, coronary angiography, right heart catheterization, and EMB within one week to exclude secondary cardiomyopathies. NIDCM was defined as LV ejection fraction <50% on echocardiography and LV end-diastolic dimension >55 mm, in the absence of coronary artery diseases, primary valvular heart disease, or secondary cardiac muscle disease caused by any known systemic condition. We excluded patients with implantable pacemakers or cardiac resynchronization therapy devices. The study protocol was approved by the Ethical Review Board of our institute, and consent was obtained from all patients.

### *Selvester QRS score*

Twelve-lead ECG was recorded at the time of scheduled admission by electrocardiograph (FCP-7541; Fukuda Denshi Co. Ltd, Tokyo, Japan). The 32-point Selvester QRS score was manually calculated by two expert cardiologists according to an algorithm, as previously reported [18]. If both scores were not matched, the QRS score was calculated by the third cardiologist in a blinded manner and finally determined. Initially, we categorized QRS complex morphology into six types: left bundle branch block (LBBB), right bundle branch block (RBBB), left anterior fascicular block (LAFB), LAFB with RBBB, LV hypertrophy, and no confounders. LV hypertrophy was defined as increased voltage according to Sokolow-Lyon or Cornell criteria and not meeting other classifications. Next, the amplitude, duration, amplitude ratio, and notch of the Q, R, and S waves were evaluated in each lead except for III or aVR. This scoring criterion was different for each QRS complex morphology, and the QRS score was individually calculated based on each criterion.

### *Hemodynamic assessment and histological analysis*

Initially, all patients underwent routine diagnostic right heart catheterization to assess hemodynamic status. After collecting hemodynamic data, we performed EMB, as follows. Biopsy samples were obtained from the septum of the right ventricle with a 6-F transcatheter bioptome. The tissue was fixed immediately in 10% buffered formalin and embedded in paraffin, and then stained with the collagen-specific dye picrosirius red (Sigma–Aldrich, St Louis, MO, USA). Three or four samples were obtained and analyzed for each patient. The collagen volume fraction (CVF), the ratio of collagen-specific staining to the total area of the myocardium in each biopsy sample, was calculated as an index for interstitial collagen using automated image analysis software (BZ 9000; KEYENCE Co. Ltd., Osaka, Japan) by two observers in a blinded manner [19].

### *Patients classification and follow-up*

Expert cardiologists followed up with optimal medical therapy according to the current guidelines for the treatment of HF [20,21]. Cardiac events were defined as a composite of cardiac death, unexpected hospitalization because of worsening HF, and lethal arrhythmia.

### *Statistical analysis*

All statistical analyses were performed by using statistical software (SPSS 18.0; SPSS, Chicago, IL, USA). Continuous variables are expressed as means ± standard deviation or as median and interquartile range, as appropriate. Parametric variables were compared using the Student's *t*-test, and non-parametric variables were compared using the Mann–Whitney *U*-test. Categorical variables are expressed as numbers (%), and were compared using the Pearson chi-squared test or Fisher's exact test. Univariate and multivariate Cox proportional hazard analysis was performed to calculate the hazard ratio and the 95% confidence interval. All potential confounders were entered in a univariate analysis, and covariates with $p < 0.05$ were retested for multivariate analysis. The best cut-off value of the Selvester QRS score was determined using the receiver operating characteristic (ROC) curve for cardiac events. Survival curves were estimated by the Kaplan–Meier method. The cardiac event-free rates were compared between the groups by the log-rank test. Spearman's rank correlation coefficient was used to examine the relationship of the Selvester QRS score with CVF. A *p*-value of <0.05 was considered statistically significant.

## Results

### *Baseline characteristics*

Baseline patient characteristics are shown in Table 1. Of all 91 patients, 66 (73%) were men, and the mean age was 53 years. Eighty-six (95%) patients were classified as having New York Heart Association functional (NYHA) class I or II. LV ejection fraction was 32 ± 9% and the plasma BNP level was 80 (43–237) pg/mL. The Selvester QRS scores of all patients were distributed from 0 to 14 points, with a mean of 4.1 points (Fig. 1). The detailed characteristics of the QRS score for each ECG type in our population are shown in Table 2. In 15 patients with LBBB, 10 (67%) patients had abnormal findings meeting the scoring criterion in aVF, 12 (80%) patients in $V_1$, and 13 (87%) patients in $V_2$. By contrast, no patients fulfilled the criteria in II or aVF in RBBB, LAFB, or LAFB with RBBB. In 35 patients with LV hypertrophy, 25 (71%) patients satisfied the criterion in $V_4$. In addition, approximately 40% of the

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