



Contents lists available at ScienceDirect

Indian Heart Journal

journal homepage: www.elsevier.com/locate/ihj

Research Brief

Prognostic implications of the electrocardiographic findings in acute myocarditis: Which is the strongest one?

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ARTICLE INFO

Article history:

Received 5 August 2020

Received in revised form

14 September 2020

Accepted 24 December 2020

Available online 30 December 2020

Keywords:

Myocarditis

Electrocardiography

ABSTRACT

Myocarditis is an inflammatory disease of the myocardium with high morbidity and mortality; however, definite prognostic factors are still unclear. Therefore, we aimed to evaluate the predictor of clinical outcomes of acute myocarditis focusing on electrocardiographic findings. The overall result of the study consists of a total of 51 patients demonstrated that wide QRS duration is a meaningful factor for predicting the fulminant course of acute myocarditis. This finding may encourage timely mechanical support resulting in better clinical outcomes.

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1. Introduction

Myocarditis is defined as an increased humoral or cellular immune response causing inflammation of the myocardium, which can be induced by various factors such as infection, autoimmune diseases, and toxins.^{1,2} Clinical manifestations of myocarditis range from chest pain to fatal ventricular arrhythmias or cardiogenic death.³ Prognostic factors for acute myocarditis are still unknown; however, several previous studies have demonstrated that reduced left ventricular ejection fraction (LVEF) or the presence of abnormal electrocardiographic parameters may predict a poor outcome in acute myocarditis.⁴ An electrocardiogram (ECG) can easily be recorded and may suggest the extent of injury to the myocardium. However, the prognostic role of ECG characteristics is still uncertain. Therefore, the aim of this study was to identify characteristic ECG findings in acute myocarditis and evaluate their prognostic values.

2. Methods

2.1. Study population

The study was designed as a single-center, retrospective registry to evaluate the predictors of acute myocarditis. We retrospectively

collected demographic and clinical data from 51 consecutive patients with acute myocarditis by reviewing the medical records from May 2010 to June 2019. The study population was divided into two groups: the fulminant group (n = 29) and the non-fulminant group (n = 22). The fulminant group was defined as the group of patients who required mechanical circulatory support, such as extracorporeal membrane oxygenation (ECMO) and/or intra-aortic balloon pump (IABP) insertion, emergent heart transplantation (HT) or cardiac deaths. Patients who recovered from the event without the need for circulatory support were included in the non-fulminant group. This retrospective study was approved by the ethical review board of our institution, and the requirement for informed consent was waived. A diagnosis of acute myocarditis was established based on the patient's clinical features, elevation of myocardiocytolysis markers, and cardiac imaging studies in accordance with the Dallas criteria.⁵

2.2. Electrocardiographic/echocardiographic analysis

At the time of admission, all patients underwent 12-lead ECG at a paper speed of 25 mm/s and standard sensitivity of 10 mm/mV which were interpreted by two cardiology specialists based on the recommendation of AHA/ACCF/HRS.^{6,7} A normal range for QRS duration was defined as less than 120 ms. We assessed the following parameters in echocardiography: LVEF and left ventricular mass using biplane Simpson's rule method, ratio of the early mitral inflow velocity to mitral annular early diastolic velocity (E/e'), left ventricular chamber size/thickness and left atrial diameter analyzed from the M-mode images of the parasternal long/short

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axis view, and the presence of pericardial effusion from the serial apical chamber view and parasternal views. As per the recommendations of the American Society of Echocardiography, regional wall motion abnormalities were evaluated using a 17-segment model.⁸

2.3. Statistical analysis

All numerical data are expressed as mean ± standard deviation for continuous variables, while categorical data are presented as percentages using the chi-square test. Comparison between the two groups was performed using Fisher's exact test or Mann–Whitney *U* test. The cumulative event-free survival rate was described according to the Kapan-Meier method, and the discrepancy between the curves was assessed with the log-rank test. A *p* value of <0.05 was considered statistically significant. Overall, data analyses were performed using statistical Package for the Social Sciences (SPSS) version 22.0.

3. Results

The baseline characteristics, laboratory, electrocardiographic and echocardiographic findings of the two groups are summarized in Table 1. No significant differences in age, sex, hypertension, and diabetes mellitus were found between the groups except for initial blood pressure, LVEF, and certain laboratory parameters. Approximately 53% of a total population underwent coronary angiographies which showed non-significant results. The most common ECG finding in the fulminant group was a bundle branch block (48.3%), while ST segment elevation (45.5%) was the most common finding in the non-fulminant group. No significant differences were found in the initial heart rate and PR and QT intervals between the groups. However, the QRS duration and QTc interval were significantly prolonged in the fulminant group compared with in the non-fulminant group.

Among the fulminant group, a total of 8 cardiac deaths and 1 case of emergent HT were observed; 25 (86.2%) and 9 patients

Table 1
Baseline characteristics of the patients with acute myocarditis (n = 51).

	Fulminant group (n = 29)	Non-fulminant group (n = 22)	<i>P</i> -value
Male (n,%)	18 (62.1%)	18 (81.8%)	0.214
Age (years)	44.8 ± 18.1	36.5 ± 20.9	0.056
HTN (n,%)	5 (17.2%)	3 (13.6%)	NS
DM (n,%)	3 (10.3%)	1 (4.6%)	0.625
Prior CAOD (n, %)	0 (0%)	0 (%)	NS
Prior CVA (n, %)	0 (0%)	0 (%)	NS
Systolic BP (mmHg)	89.0 ± 19.0	120.0 ± 23.6	<0.001
Diastolic BP (mmHg)	57.4 ± 14.2	70.7 ± 13.2	0.002
Heart rate (per minute)	100.3 ± 29.0	89.2 ± 18.7	0.123
Laboratory data			
WBC (x10 ⁶ /L)	11770.0 ± 5068.3	8087.0 ± 2561.0	0.005
AST (U/L)	188.6 ± 157.8	55.4 ± 30.5	<0.001
ALT (U/L)	108.1 ± 85.7	39.8 ± 24.1	<0.001
Total bilirubin (mg/dl)	0.88 ± 0.49	0.97 ± 0.66	0.580
BUN (mg/dl)	20.77 ± 9.60	14.38 ± 5.92	0.003
Creatinine (mg/dl)	1.31 ± 0.55	1.02 ± 0.17	0.027
CRP (mg/dL)	7.06 ± 5.61	5.30 ± 6.05	0.119
Initial CK-MB (ng/ml)	82.88 ± 140.98	21.50 ± 23.77	0.013
Initial hs-Tni (ng/mL)	24.12 ± 38.00	7.27 ± 13.65	0.011
Electrocardiographic finding			
CAVB (n, %)	3 (10.3)	0 (0)	
LBBB (n, %)	4 (13.8)	0 (0)	
RBBB (n, %)	10 (34.5)	3 (13.6)	
NSR (n, %)	1 (3.5)	6 (27.3)	
Poor R progression (n, %)	4 (13.8)	1 (4.6)	
Q wave (n, %)	1 (3.5)	0 (0)	
LVH (n, %)	1 (3.5)	1 (4.6)	
ST elevation (n, %)	4 (13.8)	10 (45.5)	
T wave inversion (n, %)	1 (3.5)	1 (4.6)	
Low voltage (n, %)	1 (3.5)	0 (0)	
Atrial flutter (n, %)	1 (3.5)	0 (0)	
PR interval (ms)	152.15 ± 23.85	155.10 ± 19.11	0.641
QRS (ms)	115.59 ± 33.05	94.27 ± 18.26	0.005
QTc (ms)	477.90 ± 39.77	444.23 ± 37.62	0.004
QT (ms)	362.07 ± 60.46	369.91 ± 35.77	0.592
Echocardiographic parameters			
LVEF (%)	41.69 ± 16.22	50.27 ± 15.52	0.037
E/e'	12.6 ± 5.6	10.3 ± 5.6	0.026
LVSD (mm)	11.27 ± 1.87	10.51 ± 2.43	0.214
LVPWd (mm)	10.41 ± 1.75	10.41 ± 2.48	0.550
LVEDs (mm)	36.79 ± 9.22	38.37 ± 10.47	0.783
LVEDd (mm)	50.17 ± 8.97	51.31 ± 8.32	0.613
LV mass	219.40 ± 74.03	213.66 ± 86.79	0.558
LA Diameter (mm)	36.51 ± 7.89	37.15 ± 6.59	0.836
Pericardial Effusion (n, %)	19 (64.3%)	11 (52.2%)	0.138

ALT: alanine transferase, AST: aspartate aminotransferase, BP: blood pressure, BUN: blood urea nitrogen, CAOD: coronary artery occlusive disease, CAVB: complete atrioventricular block, CK-MB: creatine kinase-muscle/brain, CRP: C-reactive protein, CVA: cerebrovascular accident, DM: diabetes mellitus, E/e': IVS: end-diastolic intraventricular septum, HTN: hypertension, hs-Tni: highly sensitive troponin I, LA: left atrium, LBBB: left bundle branch block, LV: left atrium, LVEDd: end-diastolic left ventricular diameter, LVEDs: end-systolic left ventricular diameter, LVEF: left ventricular ejection fraction, LVH: left ventricular hypertrophy, LVPW: left ventricular posterior wall, NSR: normal sinus rhythm, RBBB: right bundle branch block, WBC: white blood cell.

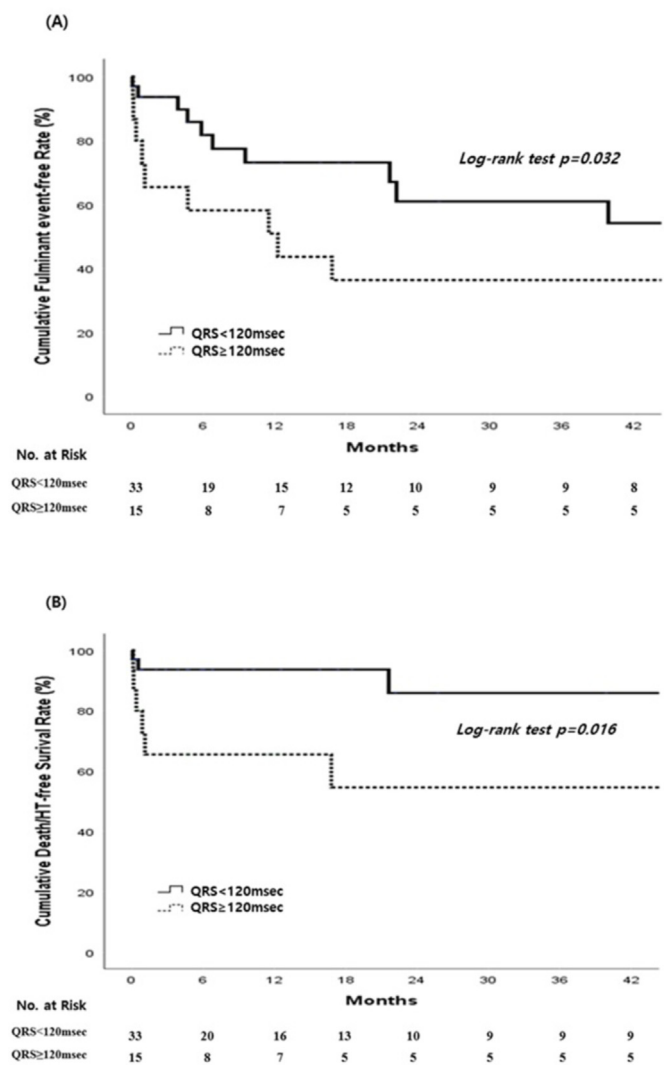


Fig. 1. Cumulative event-free survival curves in the patients with acute myocarditis grouped according to QRS duration. The figure demonstrates a significant discrepancy between two groups (QRS duration < 120 msec vs. QRS duration ≥ 120 msec) with prominent increase of cardiac death and HT in the longer QRS group.

(31.0%) underwent ECMO and IABP insertion, respectively (Supplemental Fig. 1). Most cardiac deaths were a result of cardiogenic shock with progression to multiple organ failure.

Logistic regression analyses for the fulminant course are shown in supplemental Table 1. QRS ≥ 120 ms (hazard ratio [HR]: 21.947; 95% confidence interval [CI]: 1.790–269.022; p = 0.016) remained as the only meaningful electrocardiographic variable for predicting the fulminant course after conducting multivariate analysis. A significant disparity was observed between the two groups (QRS < 120 ms vs. QRS ≥ 120 ms) with an obtrusive increase in cardiac death and HT in the prolonged QRS group (log-rank test; p = 0.016; Fig. 1).

4. Discussion

The study results revealed that significantly prolonged QRS duration and QT interval were observed in the fulminant group compared with the non-fulminant group, suggesting that initial ECG findings may be associated with a poor prognosis of acute

myocarditis. Previous studies have emphasized the importance of early recognition of the progression of acute myocarditis, as the disease course is abrupt and may result in fatal outcome.⁹ Therefore, early prediction of the fulminant course followed by aggressive treatments, are necessary in these patients. Potential risk factors for fulminant myocarditis have been assessed by prior studies^{4,10} including inflammatory indicators and echocardiographic parameters; but otherwise in the current study, we demonstrated the predictive roles of certain ECG parameters in anticipating the fulminant course. ECG findings of acute myocarditis may appear as changes in the ST segment or T wave and/or as a pathologic Q wave that may be confused with acute myocardial infarction.^{11–13} These findings may be the result of diffuse myocardial inflammation which are associated with conduction abnormalities. However, our study showed that the specific ECG findings in fulminant myocarditis are related to QRS duration rather than ST segment changes. One study¹⁰ reported both wide QRS complexes and prolonged QTc intervals as possible predictors for the fulminant course. In multivariate analysis of the present study demonstrated that the QTc interval was not a significant risk factor for the fulminant course. There are several limitations in our study. First, as this was a single-center study, the number of the participants was small. However, the total number of patients in the fulminant group was markedly higher in the present study than in prior studies, in which the majority of patients received timely ECMO support (86.2%).^{4,9,10} This strengthens the reliability of the study results. Second, this study was designed as a retrospective study. Finally, a diagnosis of myocarditis was made in accordance with the Dallas criteria⁵ not endomyocardial biopsy because of a relatively high percentage of underdiagnoses.

To conclude: Our findings suggest that prolonged QRS duration is the meaningful predictor for the fulminant course of myocarditis. Early detection using certain predictors may yield a favorable clinical outcome by encouraging timely mechanical circulatory support.

Declaration of competing interest

The authors declare no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ihj.2020.12.016>.

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