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Statistical evaluation of reproducibility of automated ECG measurements: An example from arrhythmogenic right ventricular dysplasia/cardiomyopathy clinic

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ABSTRACT

Background: Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) is characterized by delay in depolarization of the right ventricle, detected by prolonged terminal activation duration (TAD) in V1–V3. However, manual ECG measurements have shown moderate-to-low intra- and inter-reader agreement. The goal of this study was to assess reproducibility of automated ECG measurements in the right precordial leads.

Methods: Pairs of ECGs recorded in the same day from Johns Hopkins ARVD/C Registry participants [$n = 247$, mean age 35.2 ± 15.6 years, 58% men, 92% whites, 11(4.5%) with definite ARVD/C] were retrospectively analyzed. QRS duration, intrinsicoid deflection, TAD, and T-wave amplitude in the right precordial leads, as well as averaged across all leads QRS duration, QRS axis, T axis, QTc interval, and heart rate was measured automatically, using 12SL TM algorithm (GE Healthcare, Wauwatosa, WI, USA). Intrinsicoid deflection was measured as the time from QRS complex onset to the alignment point of the QRS complex. TAD was calculated as the difference between QRS duration and intrinsicoid in V1–V3. Reproducibility was quantified by Bland–Altman analysis (bias with 95% limits of agreement), Lin's concordance coefficient, and Bradley–Blackwood procedure.

Results: Bland–Altman analysis revealed satisfactory reproducibility of tested parameters. V1 QRS duration bias was −0.10 ms [95% limits of agreement −12.77 to 12.56 ms], V2 QRS duration bias −0.09 ms [−11.13 to 10.96 ms]; V1 TAD bias 0.14 ms [−13.23 to 13.51 ms], V2 TAD bias 0.008 ms [−12.42 to 12.44 ms].

Conclusion: Comprehensive statistical evaluation of reproducibility of automated ECG measurements is important for appropriate interpretation of ECG. Automated ECG measurements are reproducible to within 25%.

1. Introduction

Assessment of the reproducibility of any measurement technique in medicine is always needed, because only reproducible measurement techniques can provide reliable results. During recent years, remarkable advancements in biostatistics have been made, allowing for comprehensive evaluation of reproducibility. However, neither clinicians nor engineers are thoroughly familiar with available biostatistical methods for assessment of reproducibility. This fact motivated us to conduct a study with a comprehensive biostatistical evaluation of reproducibility.

Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) is an inherited heart disorder characterized by fibro-fatty replacement of the right ventricular myocardium and life-threatening ventricular arrhythmias [1,2]. Arrhythmias often precede gross structural abnormalities in the myocardium and can occur early in the natural history of ARVD/C [3,4]. Mutations in the genes encoding desmosomal proteins, responsible for cell-to-cell coupling via gap junctions, have been linked to ARVD/C [5]. Cell-to-cell uncoupling results in slow, heterogeneous electrical

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conduction in the right ventricular (RV) free wall and RV outflow tract, presented as the epsilon wave and QRS prolongation in the right precordial leads on a surface ECG, and as prolonged RV endocardial activation on an intracardiac electroanatomic map [6].

An International Task Force has endorsed a set of criteria for the clinical diagnosis of ARVD/C, with ECG criteria comprising an important component of the diagnostic criteria [1,2,7]. T-wave inversion in the right precordial leads (V1–V3) in individuals > 14 years of age in the absence of the complete right bundle branch block (RBBB) and the presence of the epsilon wave in the right precordial leads, were identified as two major criteria of ARVD/C diagnosis. Terminal activation duration (TAD) of QRS (distance from the S-wave nadir to the end of QRS) ≥55 ms in V1, V2 or V3 in the absence of complete RBBB was identified as a minor criterion. However, a previous study has demonstrated that manual measurements of many quantitative ECG parameters relevant to ARVD/C diagnosis, particularly QRS duration, can vary greatly between readers [8].

Automated ECG analysis represents a potentially useful alternative to manual ECG measurements. Several studies have compared the reproducibility of manual and automated measurements of averaged QRS duration on 12-lead ECGs [9,10], showing the advantage of automated ECG measurements. However, reproducibility of automated ECG measurements in the right precordial leads has not been previously studied. Presence of the epsilon wave or prolonged terminal activation might result in a local QRS prolongation in the right precordial leads, which could be measured automatically by modern ECG machines. However, only QRS duration averaged across all 12 leads is routinely reported. Local QRS duration in V1–V3, or TAD in V1–V3 are not routinely available for physicians. The goal of this study was to assess the reproducibility of automated measurements of QRS duration, TAD, and other ECG metrics on separate right precordial leads V1–V3 in ARVD/C registry participants.

2. Methods

2.1. Study population

The study population included participants of the Johns Hopkins ARVD/C Registry (www.ARVD.com). The registry consists of prospectively enrolled consecutive subjects who were referred to the Johns Hopkins ARVD/C clinic for evaluation. All patients included in the ARVD/C Registry provided written informed consent. The study was approved by the Johns Hopkins School of Medicine Institutional Review Board.

In our retrospective study, the study population included only those registry participants who had a pair of digital 12-lead ECGs recorded at rest on the same date (mean time between recordings 3.5 ± 2.5 h).

2.2. ECG recording

Serial 10-s digital ECGs (sampling rate 500 Hz, amplitude resolution 1 μV) of the study participants were extracted from the JHH ECG MUSE database (GE Healthcare, Wauwatosa, WI, USA) for subsequent analysis. All 12-lead ECGs used in the study were recorded using the GE-Marquette MAC 5000 ECG system (GE Healthcare, Wauwatosa, WI, USA) on the day of the outpatient visit. All study participants had two consecutive ECGs recorded on the same date.

2.3. ECG analysis

The ECGs were analyzed using 12SL™ algorithm by Magellan ECG Research Workstation Software (GE Healthcare, Wauwatosa, WI, USA). The ECG pairs were compared by examining various ECG parameters.

ECG parameters were measured on a "median beat". Depolarization parameters measured in the right precordial leads included intrinsicoid deflection, TAD, and QRS duration.

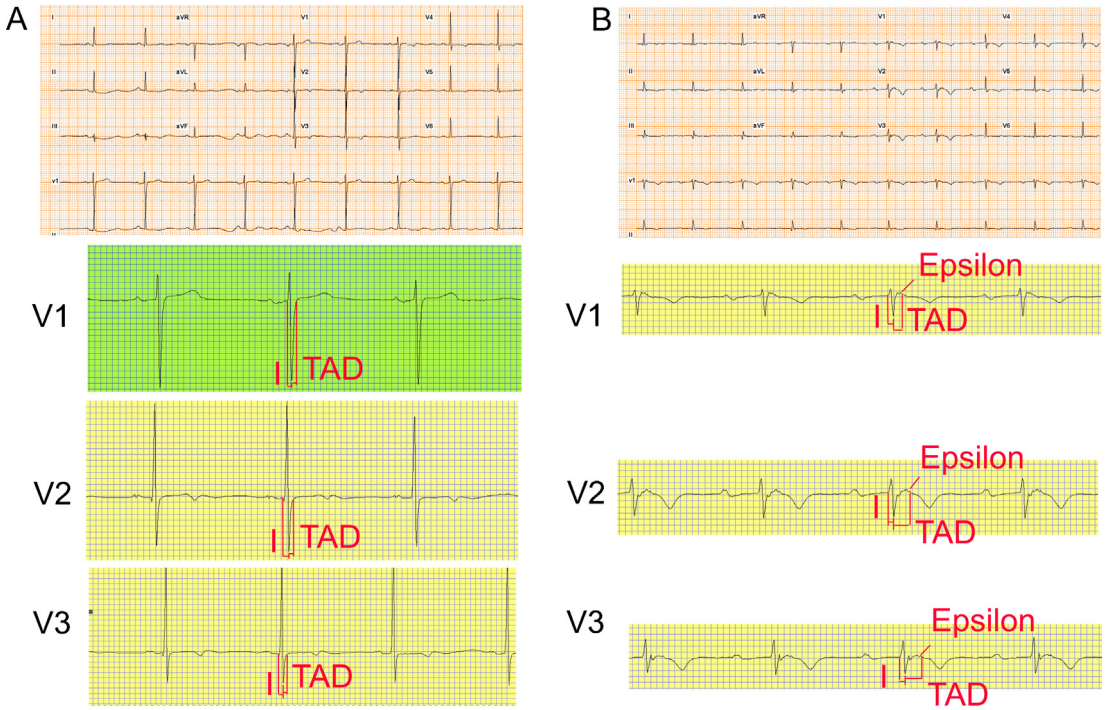

Fig. 1. Example of ECG measurements in a patient without ARVD/C (A) and in a patient with definite ARVD/C (B). Intrinsicoid deflection (I), terminal activation duration (TAD) intervals and Epsilon waves are shown in leads V1–V3 in ARVD/C patient.