



Prevalence of early repolarization pattern in patients with lone atrial fibrillation[☆]

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Abstract

Background: The objective of this study was to test the association of early repolarization pattern (ER) with lone atrial fibrillation (AF).

Methods: Electrocardiograms (ECGs) were analyzed in blinded fashion in a case–control study of 182 patients with lone AF and 182 controls without AF.

Results: Patients with lone AF and controls had similar frequencies of ER pattern (15% vs. 19%, $p = 0.40$). In patients <50 years of age, there was also no difference in the percentage of patients with ER in the AF and control groups (17% vs. 19%, $p = 0.60$). ER pattern was more common in patients with ECG voltage criteria of left ventricular hypertrophy (LVH), with ER present in 57% of patients with elevated Sokolow-Lyon voltage compared to 14% of those without ($p < 0.0001$).

Conclusions: No association could be identified between the ER pattern and lone AF in young and middle-aged patients. In this age group, ER is substantially more common in patients with elevated Sokolow-Lyon voltage criteria.

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Keywords:

Atrial fibrillation; Early repolarization; Left ventricular hypertrophy

Introduction

The early repolarization (ER) pattern, characterized by notching or slurring of the terminal QRS complex in lateral and inferior electrocardiogram (ECG) leads, has been associated with malignant ventricular arrhythmias and increased risk of sudden cardiac death [1,2]. Once thought to be a benign phenotype, long-term population studies have shown increased mortality due to cardiac causes as well as arrhythmia in subjects with this ECG pattern [3,4]. The increased predisposition to these life threatening arrhythmias in the absence of organic heart disease has been hypothesized to be due to accentuated dispersion of myocardial refractoriness, which could arise from derangements in ion channel function [5].

A variant of the KCNJ8 inward rectifying potassium channel, which is expressed in both atrial and ventricular tissue, leads to a gain-of-function mutation and has been

linked to ER [6,7] and possibly to atrial fibrillation (AF) [8]. One report identified the ER pattern in 7% of patients with idiopathic AF, including two probands with mutations in KCNJ8 [8]. In contrast, a community based study of subjects in Finland did not find a relationship between ER and AF hospitalizations [9].

While there are numerous risk factors that increase the risk for developing AF, there is a select cohort of young patients without identifiable risk factors who develop AF, termed lone AF. In such patients, a family history of AF is common, suggesting a genetic predisposition to AF [10]. In the present study, we hypothesized that patients with this type of AF would have an increased prevalence of ER pattern on 12-lead ECGs when compared to a control group. Using recently proposed diagnostic criteria for ER [11], we identified young and middle-aged patients with lone AF and analyzed their ECG for ER pattern.

Methods

Patient characteristics

A retrospective, case–control study was conducted comparing AF subjects to a control group without AF. The

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Table 1
Exclusion criteria.

Age <18 or ≥ 60
Known valvular disease (graded greater than mild or 1+ severity)
Known coronary artery disease ($\geq 70\%$ stenosis or prior myocardial infarction)
Ejection fraction (EF) <50%
Known congenital heart disease
Hypertension
Diabetes mellitus
Obstructive sleep apnea
BMI ≥ 40
Hyperthyroidism or history of thyroiditis
End stage renal disease
QRS interval > 120 msec
Wolff-Parkinson-White (WPW) syndrome
Type II 2nd degree heart block or complete heart block
History of myocarditis or pericarditis
History of rheumatic heart disease
Brugada syndrome
Poor ECG quality

study was approved by the Institutional Review Board at Weill Cornell Medical Center. All patients were identified through the electronic medical record at our institution from 2005 until 2015. Both female and male patients were included with ages ranging from ≥ 18 years old to <60 years old.

The subject group included patients with a diagnosis of AF. The control group was composed of patients diagnosed with either supraventricular tachycardia (excluding AF or atrial flutter), nonspecific palpitations, or neurally-mediated syncope. An extensive list of exclusion criteria was applied to both groups to identify patients without any organic cardiac disease or identifiable risk factors for AF (Table 1). All patients required an ECG showing sinus rhythm for inclusion. A single ECG with sinus rhythm closest to the date of the associated diagnosis was used for interpretation.

For patient selection, the database was randomized and sequentially examined for inclusion and exclusion criteria by investigators not involved with ECG interpretation. Study enrollment was completed once the goal of 182 patients was achieved in both the study and control groups, based on the sample size calculation. The AF group yielded 160 males and 22 females and the control group was gender matched to this cohort.

Baseline patient characteristics collected included age at time of reference ECG, height, weight, body mass index (BMI), co-morbidities (not included in the exclusion criteria), use of antiarrhythmic drugs, other cardiac medications (beta-blockers, calcium channel blockers, digoxin, antiarrhythmic drugs), and left ventricular ejection fraction obtained from echocardiographic data.

ECG analysis

The investigators who conducted the subject recruitment phase of the study did not analyze the index ECGs. All ECGs were de-identified and randomized for blinded analysis by two investigators. A third investigator was used for adjudication if there was disagreement in the ECG analysis. As per recently proposed diagnostic criteria [11], ER pattern was described as notching or slurring in the terminal QRS ≥ 0.1 mV above the baseline in at least 2 contiguous lateral precordial, inferior, or lateral limb leads (Fig. 1). The term J peak (Jp) defines the amplitude of the peak of a notch or the onset of a slur and was used in analysis. A stricter definition using $J_p \geq 0.2$ mV was used in a pre-defined secondary analysis. In addition to ER pattern, other manually measured ECG characteristics included the presence of left ventricular hypertrophy (LVH) by Sokolow-Lyon, Cornell voltage, and Cornell voltage product criteria [12]. Conduction intervals and heart rate were computer-generated.

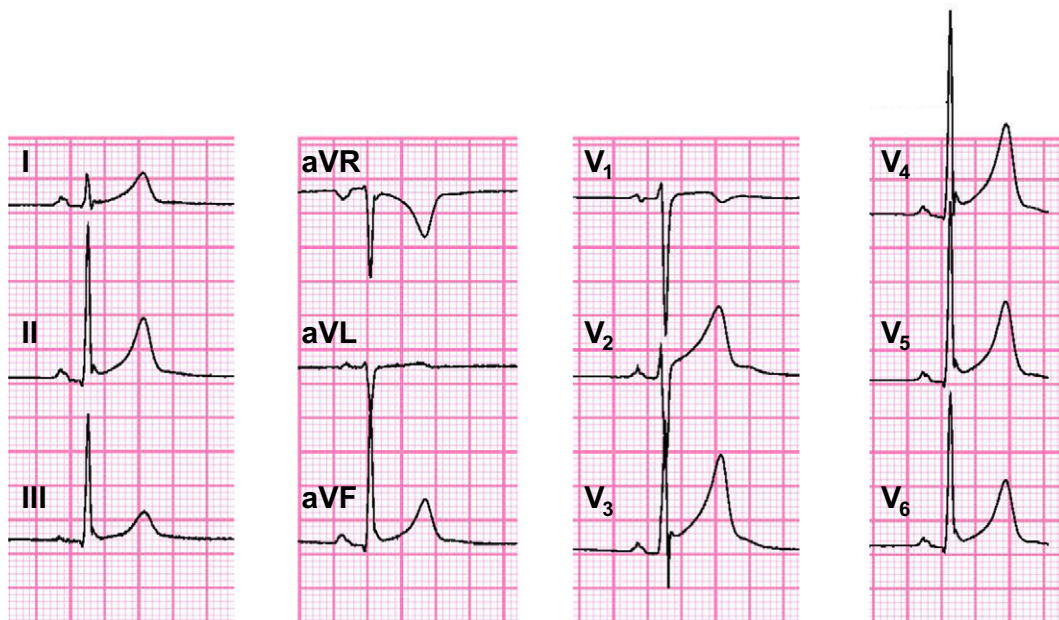


Fig. 1. Characteristic ECG from a 23 year old man demonstrating early repolarization in the lateral precordial and inferior leads, with notching of the terminal QRS. Peak J amplitude (Jp) is 0.25 mV in leads V5 and V6.

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