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Short Report

Monophasic action potential duration alternans after abrupt shortening of the cardiac cycle in humans ☆

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ABSTRACT

Background: Action potential alternans may be important in causing ventricular arrhythmias.
Methods and results: We recorded monophasic action potentials from the right ventricular endocardium in patients with persistent atrial fibrillation who underwent internal atrial defibrillation during rapid ventricular pacing. In 3 of 45 patients, monophasic action potential duration alternans was observed at a pacing cycle length ≤350 ms.
Conclusion: Action potential alternans is not a rare phenomenon (6.6%) in humans.

1. Introduction

Action potential duration (APD) alternans is a well-recognized phenomenon that occurs at rapid rates of stimulation and after an abrupt shortening of the cardiac cycle [1–8]. When the rate of stimulation is constant, the short action potential during alternans is followed by a longer diastolic interval and the long action potential is followed by a shorter diastolic interval. These differences in diastolic interval may be responsible for the occurrence and maintenance of APD alternans. Alternation in APD may result in alternation of the refractory period, which may become the basis of arrhythmias. The demonstration of ventricular APD alternans has been confined to experimental animal models [1,8–13], with the phenomenon being documented in only a few humans [14,15]. We sought to determine whether an increase in heart rate could induce APD alternans during clinical electrophysiologic study.

2. Methods

2.1. Patients

This study included 45 consecutive patients (28 men, 17 women; mean age 58.8 ± 12.0 years, range 34–77 years) with nonvalvular chronic atrial fibrillation (AF) lasting > 2 months (15.5 ± 17.1 months, range 2–66 months) and were referred to Nihon University Hospital for cardioversion of sustained AF between December 1999 and July 2004. All had failed external cardioversion and had agreed to internal cardioversion. Exclusion criteria were a corrected QT interval of > 440 ms and left ventricular ejection fraction of < 45%. The study protocol, comprising internal atrial defibrillation followed by electrophysiologic study, was approved by the Clinical Research Committee of Nihon University Hospital on November 1, 1999 (approval #45), and written informed consent was obtained from all patients.

2.2. Internal cardioversion

Internal cardioversion was performed by delivering a shock between two 6F decapolar electrodes (electrode length: 5 mm; interelectrode distance: 2 mm; ELECATH, Rahway, NJ, USA) positioned in the right atrial appendage and distal coronary sinus. Biphasic shocks of 3 ms/3 ms were used for cardioversion of the AF (HVS-02; Ventritex, Sunnyvale, CA, USA). Biphasic shocks were started at 100 V/100 V and were increased by increments of 50 V until cardioversion occurred. All 45 patients were successfully cardioverted at a mean energy of 8.6 ± 3.5 J without complication.

2.3. Study protocol

Antiarrhythmic drug treatment (excluding digitalis, beta-blockers, and calcium channel blockers) was discontinued at least 5

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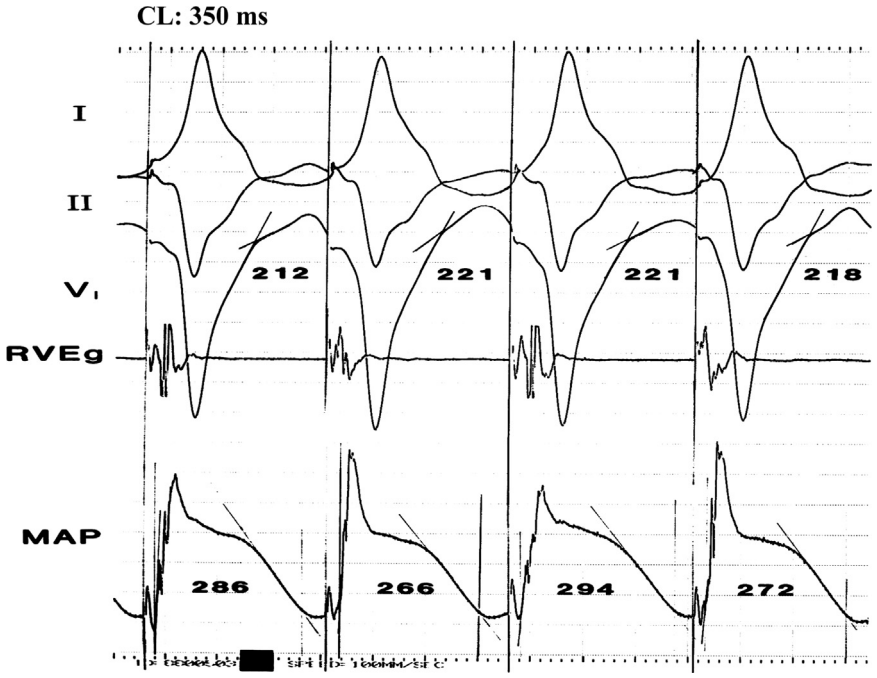

Fig. 1. Monophasic action potential (MAP) recorded from the right ventricle (RV) during right ventricular pacing at a cycle length of 350 ms. Note that RV MAP duration showed alternans (286–266–294–272 ms) without apparent QRS duration change.

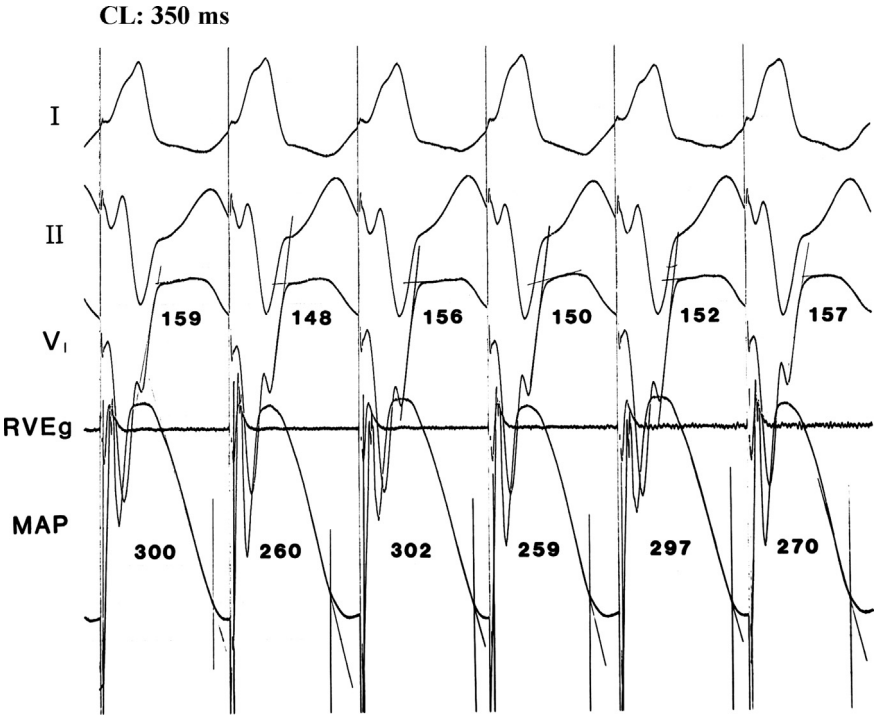

Fig. 2. Monophasic action potential (MAP) recorded from the right ventricle (RV) during right ventricular pacing at a cycle length of 350 ms. Note that RV MAP duration showed alternans (300–260–302–259–297–270 ms) without apparent QRS duration change.

half-lives before the electrophysiologic procedure. A 7F Franz-combination catheter (EPT Ltd., Sunnyvale, CA, USA) was inserted through the right femoral vein, and monophasic action potential (MAP) duration (MAPD) was recorded by pressing the Franz catheter against the right ventricular apex. MAP signals were amplified at a filter setting of 0.05–500 Hz. Ventricular pacing was performed from the proximal electrode pair of the Franz® catheter at twice the diastolic threshold strength and a 2-ms pulse duration. MAPD was measured as the interval along a line horizontal to the diastolic baseline from the steepest part of the MAP upstroke to the level of 90% repolarization [16]. The right ventricle (RV) was paced at cycle lengths (CLs) of 600, 500, 400, 350, 300, and 275 ms for 120 beats at each CL. Each pacing was interrupted by 10 s of sinus rhythm. When MAPs became unstable or small during pacing, we pushed the Franz catheter against the RV wall at a location within 10 mm of the previous position until stable MAPs could be recorded. RV MAPs were recorded during atrial pacing at a filter setting of 0.05–500 Hz. MAPD at each pacing CL was measured from the onset of the steep

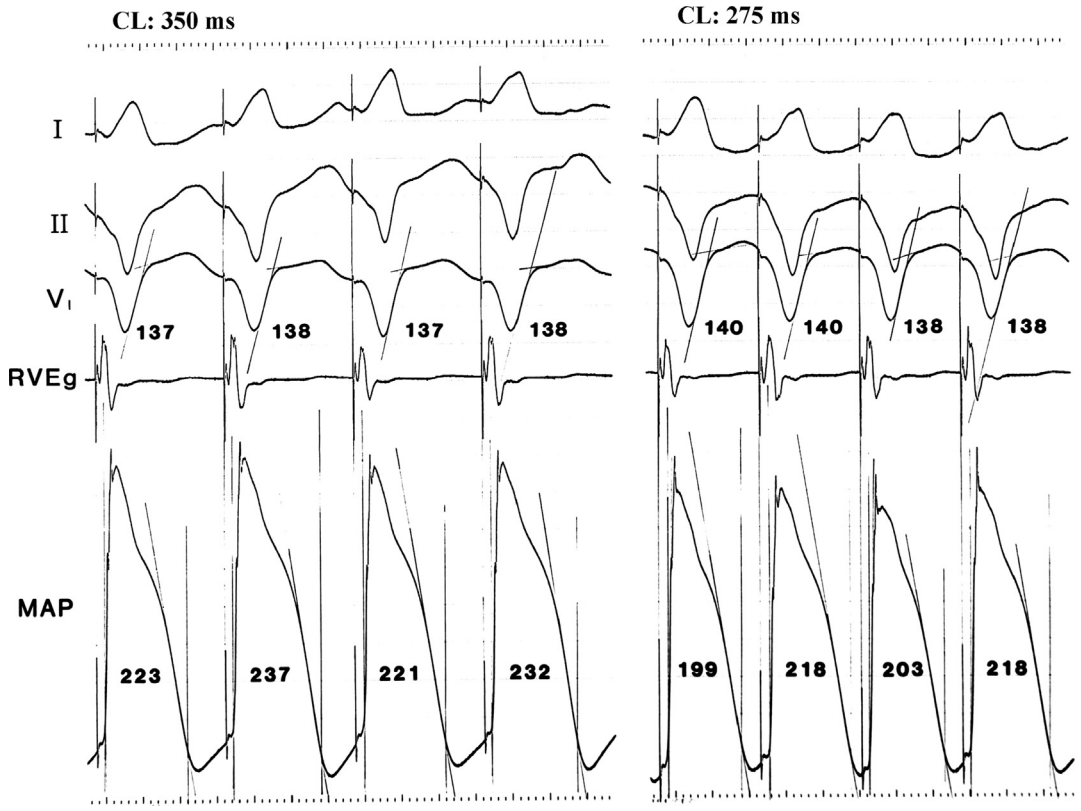

Fig. 3. Monophasic action potential (MAP) recorded from the right ventricle (RV) during right ventricular pacing at cycle lengths of 350 and 275 ms. Note that RV MAP duration showed alternans (233–237–221–232 ms at a pacing cycle length of 350 ms, 199–218–203–218 ms at a pacing cycle length of 275 ms) without QRS duration change.

upstroke of the MAP to the intersection between the diastolic baseline and a tangent placed on the phase 3 repolarization. Ventricular myocardial conduction time was assessed by measuring total QRS duration in lead V1 or lead II, with the lead being chosen according to the most clearly defined QRS-ST junction. QRS duration was measured from pacing stimulus onset to the end of the QRS complex, which was defined as the intersection of tangents to the ST segment and the major terminal deflection of the QRS complex (Fig. 1). MAPD alternans was defined as beat-to-beat changes of >10 ms lasting >10 consecutive beats at the beginning of the new pacing rates.

3. Results

RV MAPD alternans was observed (Figs. 1–3) during RV pacing in 3 of the 45 patients. These 3 patients were among the oldest (77, 75, and 71 years) in the study group, and 2 of the 3 patients were women. Patient 1 (77-year-old woman) showed MAPD alternans at pacing CLs of 350 and 300 ms (Fig. 1). Patient 2 (75-year-old man) showed MAPD alternans at a CL of 350 ms (Fig. 2). The pacing CL was not decreased in this patient because of marked MAPD alternans at this CL. Patient 3 (71-year-old woman) showed MAPD alternans at pacing CLs of 350, 300, and 275 ms (Fig. 3). QRS duration did not alternate at the pacing CLs at which MAPD alternans was observed in these 3 patients.

4. Discussion

We observed ventricular action potential alternans in 3 of 45 patients (6.7%) during rapid ventricular pacing. MAPD alternans in these 3 patients was observed at the beginning of pacing and lasted for approximately 5 s, and the duration of MAPD alternans increased at the shorter pacing CL in patients 1 and 3. MAPD alternans for a short time (<10 beats) was observed in some other patients, but we did not consider these patients as MAPD-alternans positive. Occurrence of APD alternans has been well documented at rapid rates of stimulation and after abrupt shortening of the cardiac cycle in in-vitro and in-vivo animal studies [1–13]. Sutton et al. reported action potential alternans from the left ventricular epicardium before bypass surgery in 3 of 36 patients (8.3%) undergoing routine cardiac surgery [14]. We reported action potential alternans in the RV outflow tract in a patient with asymptomatic Brugada syndrome at a pacing CL of 400 ms [15]. QRS wave and ST-T wave alternans were not observed when RV MAP alternans was recorded in the present study. Sutton et al. speculated that alternans is localized to small areas and, as such, by virtue of the recording technique, has been underestimated in the patient population as a whole [14]. The localized nature of this phenomenon and/or small change in the APD may explain the absence of any evidence of alternans on routine electrocardiography during atrial or ventricular pacing and suggests that clinical electrocardiography may not detect this potentially pre-arrhythmic condition in clinical settings.

5. Conclusion

Action potential alternans is not a rare phenomenon during rapid pacing in humans.

Conflict of interest

Authors declare no conflict of interest.

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