Slow Heart Rate Predicts New Occurrence of Atrial Fibrillation

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Background	This study aims to investigate the relation between baseline heart rate and new occurrence of AF in patients with mild symptoms.
Methods	Patients without pre-existing AF or structural heart disease who underwent 24-hour electrocardiogram (ECG) monitoring for palpitations, dizziness or syncope were followed up for new-onset AF.
Results	428 patients (mean age 66.6±10.2 years, 43.7% male) were classified according to the average heart rate into four quartiles (1st quartile: <63 beat per minute (bpm); 2nd quartile: 63-70 bpm; 3rd quartile 70-77 bpm; and 4th quartile: >77 bpm). There were no significant differences in gender, prevalence of diabetes, hypertension, left ventricular ejection fraction, or medications but a higher prevalence of coronary artery disease was noted among patients in the lower quartiles of average heart rate. After a mean follow-up of 5.8±1.8 years, 60 patients (14.0%) developed new-onset AF. The annual incidence of new-onset AF was highest amongst those at the lowest quartile of average heart rate (9.39%/year) as compared to those amongst other quartiles. Cox regression analysis revealed that increasing age, decreasing quartile of average heart rate, and the use of calcium channel blocker were associated with increased risk of new-onset AF.
Conclusions	Average heart rate predicts new AF.
Keywords	Heart rate • Bradycardia • Atrial fibrillation • Symptoms • 2-hour ECG

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia encountered in clinical practice, [1] and is associated with an increased risk of ischaemic stroke, congestive heart failure, and death [1–7]. It has been estimated that around 1% of the overall population suffer from AF [8]. With an increasingly ageing population, the absolute number of AF patients is expected to increase by two- to three-fold in the next 20-30 years [9]. Conventional risk factors for AF include male gender, advanced age, diabetes, hypertension, hyperthyroidism and the presence of structural heart diseases such as coronary heart disease, valvular heart disease, and congestive heart failure [6,8,10–14]. More recently, certain benign electrographic phenomena such as prolonged PR-interval [15] and frequent premature atrial complex [16–21] have also been shown to contribute to incident AF. On the other hand, although a higher and irregular heart rate are the cardinal features of AF, it remains uncertain whether a lower and higher baseline average heart rate are associated with future development of AF. The aim of this study was to investigate the relation between the baseline heart rate and the new occurrence of AF in patients with symptoms suggestive of possible cardiac arrhythmia.

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Methods

Patients

Between July 2002 and December 2003, 743 consecutive patients with palpitations, dizziness or syncope were referred to our non-invasive cardiology laboratory for elective 24-hour electrocardiography (ECG) monitoring. Patients were excluded if they had previously documented AF or AF diagnosed during 24-hour ECG monitoring, high-grade atrio-ventricular block, pacemaker or implantable cardioverter defibrillators, chronic rheumatic heart disease, history of congestive heart failure, or ischaemic stroke. The final analysis thus involved 428 patients.

Study Design

Demographic data, cardiovascular risk factors, indications for 24-hour ECG monitoring and medications were recorded. Hypertension was defined as resting systolic or diastolic blood pressure ≥140/90 mmHg on two occasions or taking anti-hypertensive medications. Diabetes mellitus was defined as serum fasting glucose ≥7.0mmol/l or taking anti-diabetic medications. Smoking status was recorded as smoker (past and current) or non-smoker. 24-hour ECG monitoring (GE Marquette SEER digital system) was performed to assess heart rate. All 24-hour ECG recordings were reviewed and edited manually. Recordings had to exceed 20 hours and be of good quality to be accepted for analysis by two independent cardiologists. Patients were prospectively followed up in our medical and/or cardiac outpatient clinic on a quarterly basis. During follow-up, all patients were interviewed in person for the development of new symptoms or change in previous symptoms, and had physical examinations performed by registered physicians. Standard 12-lead ECG and 24-hour Holter monitoring would be offered when there were signs or symptoms suggestive of new-onset AF. The primary endpoint of new occurrence of AF was defined as AF documented by at least two standard 12-lead ECGs at least four hours apart. This study received approval from the Clinical Research Ethics Committee of Queen Mary Hospital.

Statistical Analysis

Continuous variables are expressed as mean ± SD. Statistical comparisons were made using Student's t test or Pearson Chi-squared test, as appropriate. Patients were stratified into quartiles according to the minimal heart rate, maximal heart rate and average heart rate recorded during 24-hour ECG monitoring. Kaplan-Meier survival functions and the log-rank test were used to compare the survival distributions among groups. Logistic regression analyses were used to calculate the odds ratios (ORs) and 95% confidence intervals (CIs) of new-onset AF amongst patients at different heart rates as well as other demographic factors. Variables with P-value ≤ 0.1 were included in the multivariate model. Calculations were performed using SPSS software (version 18.0). A *p*-value <0.05 was considered statistically significant.

Results

A total of 428 patients were included in the final analysis. Table 1 summarises the clinical characteristics of the study population. The mean age was 66.6±10.2 years and 43.7% patients were male. 187 patients (43.7%) had hypertension, 73 patients (17.1%) had diabetes mellitus, and 75 patients (17.5%) had coronary artery disease. The main indication of 24-hour ECG monitoring was palpitation (54.9%). The mean and median average heart rate were 69.9±10.6 bpm and 70 bpm (IQR: 63 bpm and 77 bpm). The mean and median minimal heart rate were 49.8±10.1 bpm and 50.0 bpm (IQR: 44 bpm and 55 bpm); whereas the mean and median maximal heart rate were 109.8±21.6 bpm and 109 bpm (IQR: 97 bpm and 122 bpm) respectively. There were no significant differences in gender, prevalence of diabetes, hypertension, left ventricular ejection fraction, or medications among quartiles. Patients at lower quartiles of average heart rate nonetheless had higher prevalence of coronary artery disease and premature atrial complex (PAC) ≥100 beats per day on Holter recordings than those at higher quartiles.

Association with New Occurrence of AF

After a mean follow-up of 5.8±1.8 years, 60 patients (14.0%) of the entire cohort developed new-onset AF. Specifically, the annual incidence of AF was highest amongst those at the lowest quartile of average heart rate (9.39%/year), which decreased progressively with increasing quartiles of average heart rate (8.05%/year in patients at the second quartile and 3.05%/year in patients at the third quartile). However, amongst patients at the highest quartile of average heart rate, the annual incidence of new-onset AF was 3.24%/year, which was similar to that of the third quartile (Figure 1B). Similar trends in annual incidence of AF were also observed across different quartiles of minimal heart rate and maximal heart rate (Figure 1A and 1C). Figure 2 depicts the Kaplan–Meier AF-free survival in patients at different quartiles of average heart rate, showing a significantly lower AF-free survival among those at the first and second quartiles as compared to those at the third and fourth quartiles of average heart rate (p<0.01). Table 2 summarises the ORs and 95% CIs of individual factors that might contribute to new-onset AF using logistic regression analyses. Of these, only increasing age, decreasing quartile of average heart rate, PAC ≥100 beats per day and the use of calcium channel blockers were associated with increased risk of new-onset AF in both univariate and multivariate models.

Discussion

We studied the relationship between the baseline heart rate and the new occurrence of AF in patients with mild symptoms. Our results showed that the incidence of new-onset AF was the highest among patients at the lowest quartile of average heart rate. Furthermore, increasing age, decreasing quartile of average heart rate, PAC ≥100 beats per day and the use of