Prevalence and Prognostic Significance of Runs of Premature Atrial Complexes in Ischemic Stroke Patients

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Background and Purpose: Runs of premature atrial complexes (PACs) are common in stroke patients and perceived to be clinically insignificant, but their prognostic significance is unclear. This study investigated the association between runs of PACs in ischemic stroke patients and the risk of recurrent ischemic strokes/transient ischemic attacks (TIAs) or death. *Methods:* The study included consecutive patients admitted with an ischemic stroke from August 2008 to April 2011. Patients with known and newly detected atrial fibrillation were excluded. Runs of PACs were defined as 3 or more PACs lasting less than 30 seconds during 48 hours of continuous inpatient cardiac telemetry. The patients were followed for 4 years or until death, whichever came first. They were stratified according to stroke severity. The combined primary endpoint was a recurrent ischemic stroke/TIA or death. *Results:* Of the 565 patients included in the study, 28% had runs of PACs. Patients with runs of PACs were likely to be older, female, and to have experienced more severe strokes. During the follow-up, 210 (37%) patients had a recurrent ischemic stroke/TIA (n = 73) or died (n = 137) respectively. Among the 489 patients who had mild-to-moderate strokes, runs of PACs were associated with recurrent ischemic strokes/TIAs or death (hazard ratio = 1.47; 95% CI 1.06-2.04; $P = .023$). *Conclusion:* Runs of PACs were frequent in patients with acute ischemic strokes and sinus rhythm, and they were independently associated with an increased risk of recurrent ischemic strokes/TIAs or death in patients with mild-to-moderate strokes. **Key Words:** Atrial fibrillation—cardiac monitoring—ischemic stroke—prognosis—premature atrial complexes.

Introduction

Strokes are the second-leading cause of death worldwide, and often leave survivors permanently disabled, resulting in large socioeconomic costs.[1] The most severe ischemic strokes tend to be in patients with atrial fibrillation (AF),[2] which is a well-known risk factor for ischemic stroke.[3,4] Cohort studies of healthy individuals and stroke patients have shown that both excessive premature atrial complexes (PACs) and short runs of PACs are risk factors for having or developing AF.[5-9] Nevertheless, no causal relationship has been demonstrated between excessive PACs/runs of PACs and AF, and it is unknown whether the prognosis of ischemic stroke patients with PACs is the same as that of ischemic stroke patients with AF.[2]

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Runs of PACs of less than 30 seconds have been recorded among stroke patients.[6,10] These are perceived to be clinically insignificant, but their prognostic value is unknown. To determine the potential prognostic significance of runs of PACs in ischemic stroke patients without AF, this study investigated the association between the prevalence of runs of PACs and the risk of recurrent ischemic strokes/transient ischemic attacks (TIAs) or death.

Methods

Population and Cardiac Monitoring

This was a retrospective cohort study, including patients with an acute stroke and who were consecutively admitted to the stroke unit at Odense University Hospital Svendborg between August 1, 2008 and April 1, 2011. The patients were identified in the Danish Stroke Registry (DSR), which is a nationwide validated database set up to monitor the quality of care in stroke patients.[11] Participation is mandatory for all Danish hospitals that treat acute stroke. Strokes were defined according to the criteria of the World Health Organization.[12] Hemorrhagic and ischemic strokes were distinguished based on computed tomography and magnetic resonance imaging scans, and all patients with hemorrhagic strokes were excluded.

Information on the heart rhythm was evaluated reviewing patient telemetric records and patient records. To identify silent AF, all patients with a suspected stroke and without known AF routinely underwent an electrocardiogram (ECG) on admission, followed by 48 hours of continuous inpatient cardiac telemetry (CICT). During admission, a cardiologist reviewed the ECG and CICT and reported whether runs of PACs and AF had occurred. Runs of PACs were defined as 3 or more consecutive PACs, with an accelerated cycle length lasting less than 30 seconds. AF was defined according to the guidelines of the American College of Cardiology/American Heart Association as an arrhythmia lasting 30 seconds or more.[13] Patients with a history of AF, AF on the initial ECG or CICT, or absence of telemetry data were excluded. Patients without a Danish civil registration number were also excluded. The included patients were divided into those with and without runs of PACs. Additional baseline data on the following were obtained from the DSR: previous stroke, hypertension, diabetes mellitus, previous myocardial infarction (MI), and Scandinavian Stroke Scale (SSS) score. The SSS is a validated and widely used neurological stroke scale in Scandinavia that evaluates the stroke severity on a score ranging from 0 to 58, where 58 indicates a normal score.[14] A severe stroke was defined as an SSS score of less than or equal to 25, and a mild-to-moderate stroke was defined as an SSS score of more than 25, as previously used by others.[15] The risk factors were all reported within 24 hours of admission.

Follow-Up

Follow-up started on the day of admission or the date of stroke occurrence if the patient was already hospitalized with another diagnosis. All the patients were followed up for 4 years or until death, whichever came first.

Data on incident AF, recurrent ischemic strokes/TIAs, and death were obtained from discharge letters from the hospital, the national Civil Registration System, and patient records. The Civil Registration System is a national database with personal information on individuals who are resident in Denmark. All data are reported within 2 weeks. Patient records were surveyed to register any admissions to other hospitals in the country during the study period.

The primary combined endpoint was a recurrent ischemic stroke/TIA or death. Further endpoints were death, a recurrent ischemic stroke/TIA, and AF. The study was approved by the Board of the DSR, the Danish Data Protection Agency, and the Danish Health and Medicines Authority, and was registered at Clinicaltrials.gov with the ID: NCT02610803.

Statistical Analysis

Continuous variables with a normal distribution were compared using a *t*-test. The data are presented as means ± standard deviation. Data not normally distributed were compared using the Kruskal–Wallis test, and the data are presented as medians, with interquartile ranges. A chi-square test was used for a comparison of categorical variables.

The Kaplan–Meier survival estimator was used to model the risk of recurrent ischemic strokes/TIAs or death in the 2 groups, and the log-rank test was used to test whether there were any differences between the groups. A Cox proportional hazards model was used to estimate the hazard ratios of runs of PACs in relation to the primary combined endpoint and to the endpoint of death in crude and adjusted models.

To determine the association between runs of PACs and the endpoint of recurrent ischemic stroke/TIA, and AF, the Fine–Gray regression model was used, with death treated as a competing risk.[16]

All the models were adjusted for age and sex. Other covariates were only entered into the model if $P \leq .1$ in a univariate analysis. The included covariates are specified under each table. The analyses were restricted to patients without missing values. All analyses were repeated including only patients with mild-to-moderate ischemic strokes, as we expected patients in the 2 SSS score groups to have markedly dissimilar mortality rates during follow-up. The Kaplan–Meier survival estimator was used to estimate mortality rates according to stroke severity. We used Schoenfeld residuals to verify the proportional hazard assumption and performed stratified analyses when appropriate. P values $< .05$ were considered statistically significant. Statistical analyses were