Excessive Premature Atrial Complexes and the Risk of Recurrent Stroke or Death in an Ischemic Stroke Population

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Background: Our aim was to investigate the association of premature atrial complexes and the risk of recurrent stroke or death in patients with ischemic stroke in sinus rhythm. *Methods:* In a prospective cohort study, we used 24-hour Holter recordings to evaluate premature atrial complexes in patients consecutively admitted with ischemic strokes. Excessive premature atrial complexes were defined as >14 premature atrial complexes per hour and 3 or more runs of premature atrial complexes per 24 hours. During follow-up, 48-hour Holter recordings were performed after 6 and 12 months. Among patients in sinus rhythm, the association of excessive premature atrial complexes and the primary end point of recurrent stroke or death were estimated in both crude and adjusted Cox proportional hazards models. We further evaluated excessive premature atrial complexes contra atrial fibrillation in relation to the primary end point. *Results:* Of the 256 patients included, 89 had atrial fibrillation. Of the patients in sinus rhythm (n = 167), 31 had excessive premature atrial complexes. During a median follow-up of 32 months, 50 patients (30% of patients in sinus rhythm) had recurrent strokes (n = 20) or died (n = 30). In both crude and adjusted models, excessive premature atrial complexes were associated with the primary end point, but not with newly diagnosed atrial fibrillation. Compared with patients in atrial fibrillation, those with excessive premature atrial complexes had similarly high risks of the primary end point. *Conclusions:* In patients with ischemic stroke and sinus rhythm, excessive premature atrial complexes were associated with a higher risk of recurrent stroke or death. **Key Words:** Atrial fibrillation—ischemic stroke—prognosis—premature atrial complexes.

Introduction

Stroke is related to severe disabilities and a high risk of stroke recurrence and death.[1,2] A major risk factor is atrial fibrillation (AF),[3] which may, if paroxysmal, be difficult to diagnose. AF is thought to be triggered by atrial ectopic beats originating predominantly from the area around the pulmonary veins.[4] Such premature atrial complexes (PACs) presenting singly or as short runs are common findings on electrocardiograms (ECGs) and are typically considered harmless. However, they have recently been investigated in both healthy adults and patients with stroke for the prediction of subclinical AF.

Increased atrial ectopic activity has been shown to be correlated with increased risk of AF,[5-9] although no causal relationship has been demonstrated. Among healthy adults,

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a correlation was found between excessive PACs (ePACs) and stroke, beyond incident AF,[10] and with a high risk of death,[11,12] but the prognostic impact of PACs in patients with ischemic stroke is not fully elucidated. In particular, it is unknown whether the prognosis for patients with ischemic stroke with PACs is the same as that for patients with ischemic stroke and AF.[3]

The aim of the study was to investigate whether increased atrial ectopic activity is associated with an increased risk of death, recurrent stroke, and AF in patients with ischemic stroke and sinus rhythm (SR), and to compare prognoses in patients with high burdens of PACs and patients with AF.

Methods

Study Design

This prospective single-center observational cohort study complies with the Declaration of Helsinki and was approved by the regional Ethics Committee. Before inclusion, all patients gave written informed consent directly or through a surrogate when appropriate. The study was registered at Clinicaltrials.gov with the unique identifier NCT02180542.

Patients

Patients admitted to this study were >18 years and admitted with acute ischemic stroke at the stroke unit of Svendborg Hospital from 2012 to 2014. Strokes were defined according to the criteria of the World Health Organization,[13] and patients were included within 96 hours of stroke onset. Hemorrhagic and ischemic strokes were distinguished based on computed tomography and magnetic resonance imaging scans. Patients with hemorrhagic strokes were excluded. Further exclusion criteria are listed in Figure 1.

Each patient underwent a 12-lead ECG. As part of standard care, patients presenting in SR underwent 48 hours of continuous inpatient cardiac telemetry (CICT) to detect AF. To evaluate PACs, each patient without AF had a subsequent 24-hour Holter recording (Spacelabs Healthcare Lifecard CF, Issaquah, WA) performed 2-4 days after enrollment. In addition, a standard transthoracic echocardiography study was performed in all patients.

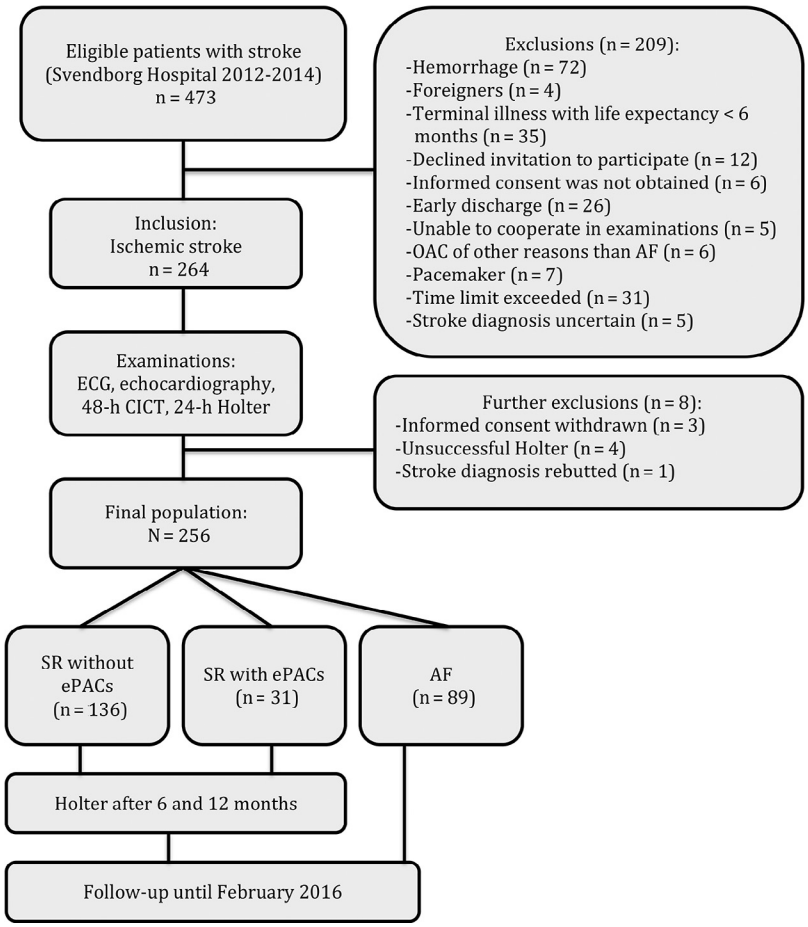

Figure 1. *Method flowchart.* Abbreviations: *AF, atrial fibrillation; CICT, continuous inpatient cardiac telemetry; ECG, echocardiogram; ePACs, excessive PACs; OAC, oral anticoagulant treatment; PAC, premature atrial complex; SR, sinus rhythm.*