Predicting Paroxysmal Atrial Fibrillation in Cerebrovascular Ischemia Using Tissue Doppler Imaging and Speckle Tracking Echocardiography

Flemming Javier Olsen, MB,* Peter Godsk Jørgensen, MD,*† Rasmus Møgelvang, MD, PhD,* Jan Skov Jensen, MD, PhD, DMsc,*† Thomas Fritz-Hansen, MD,* Jan Bech, MD, PhD,* and Tor Biering-Sørensen, MD, PhD*‡

Background: Often the underlying cause of cerebral ischemia (CI) cannot be found during a routine diagnostic investigation, but paroxysmal atrial fibrillation (PAF) could be the culprit. *Aim:* The objective of the study is to investigate whether advanced echocardiography improves the diagnostic approach for PAF in CI. *Methods:* The study included 286 CI patients with an echocardiogram in sinus rhythm. Patients were divided by PAF occurrence (PAF: n = 86, non-PAF: n = 200). PAF was defined as 1 or more reported episodes of atrial fibrillation.Echocardiograms consisted of conventional measures, tissue Doppler imaging (TDI), and speckle tracking. TDI was performed to acquire myocardial peak velocities during systole/ventricular contraction (global *s*′), early diastole/ventricular filling (global *e*′), and late diastole/atrial contraction (global *a*′). Speckle tracking was performed for myocardial strain analysis, thereby retrieving global longitudinal strain and global strain rate (*s*, *e*, *a*) values. *Results:* Patients with PAF exhibited significantly impaired atrial contractile measures: global *a*′ (–7.0 cm/second versus –5.7 cm/second, $P < .001$) and global strain rate *a* (.97 second^{-1} versus .81 second^{-1}, $P < .001$). Both were univariable markers of PAF, and along with age remained the only independent significant determinants of PAF after multivariable logistic regression. Area under the curve (AUC) for age, global *a*′, and global strain rate *a* significantly exceeded AUC for age alone (.79 versus .76, $P = .032$). Cutoff values with the highest sensitivity and specificity for these 3 parameters improved the diagnostic accuracy (sensitivity = 97%, specificity = 32%, negative predictive value = 95%, and positive predictive value = 38%). *Conclusions:* Atrial contractile measures by advanced echocardiography are significant determinants of PAF in CI. However, there is no discriminatory power to make them clinically useful at the current moment.
Key Words: Ischemic stroke—atrial fibrillation—echocardiography—cardioembolic stroke—speckle tracking—tissue Doppler imaging.

From the *Department of Cardiology, Herlev Gentofte Hospital, University of Copenhagen, Denmark; †Institute of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark; and ‡Department of Medicine, Cardiovascular Medicine Division, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts.

Received July 2, 2015; revision received September 29, 2015; accepted October 6, 2015.

This study received funding from Carpenter Sophus Jacobsen and Wife Astrid Jacobsen's Foundation, Vera and Flemming Westerberg's Foundation, and The Danish Heart Foundation. The sponsors had no role in the study design, data collection, data analysis, data interpretation, or writing of the manuscript.

Address correspondence to Flemming Javier Olsen, MB, Department of Cardiology, Herlev Gentofte Hospital, University of Copenhagen, Niels Andersens Vej 65, 2900 Hellerup, Denmark. E-mail: flemming.j.olsen@gmail.com.

1052-3057/$ - see front matter

http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2015.10.004

Introduction

Cerebral ischemia (CI) is the second leading cause of death worldwide, imposes a major socioeconomic burden, and can have grave repercussions for patients and relatives.[1]

Following a CI, a comprehensive diagnostic workup for unraveling the underlying cause is commenced. Unfortunately, in a third of cases the etiological factor cannot be determined and the event is designated a cryptogenic stroke.[2-4] However, recent trials utilizing insertable cardiac monitors have revealed nearly a third of these patients to have paroxysmal atrial fibrillation (PAF).[5] This arrhythmia confers a 5-fold risk of developing ischemic stroke,[6] and is associated with more severe morbidity and higher mortality rates than strokes of other causation.[7] Accordingly, the identification of PAF following CI is important because the secondary stroke prevention changes from antiplatelet (AP) to anticoagulant (AC) therapy. Guidelines for the monitoring of patients with unexplained stroke have recently been refined to recommend at least 30 days of monitoring.[8] However, the Cryptogenic Stroke and underlying Atrial Fibrillation trial,[5] may support the application of insertable monitors in the near future. Seeing as not all patients benefit from insertable cardiac monitors and because such monitors are invasive, a risk assessment for PAF in CI patients is warranted to select those who may gain mostly from prolonged monitoring.

Many CI patients and particularly those with cryptogenic strokes will have an echocardiogram performed as part of the diagnostic investigation.[9] Novel echocardiographic modalities, including color tissue Doppler imaging (TDI) and myocardial deformation by speckle tracking echocardiography (STE), may provide some suitable markers of PAF and thereby help augment the detection of PAF.

Methods

Population

This was a retrospective study consisting of patients admitted with either a transient ischemic attack or ischemic stroke at Gentofte Hospital, University of Copenhagen.[10] The patients were identified by International Classification of Diseases 10 codes for transient ischemic attack and ischemic stroke (DI63, DI65, DI66, DG45). These were then cross-referenced with the echocardiographic database at Gentofte Hospital. Only patients who had an echocardiographic examination performed within the period of 3 months before their index stroke up until 6 months after their stroke were considered eligible, leaving 371 patients for inclusion. Patients in atrial fibrillation (AF) rhythm during the echocardiographic examination were excluded. Patients whose medical files specified that they suffered from persistent AF were also excluded. Additionally, some patients were excluded due to poor image quality, and some were excluded if the underlying cause of their index stroke was apparent (i.e., endocarditis and periprocedural stroke; see Fig 1).

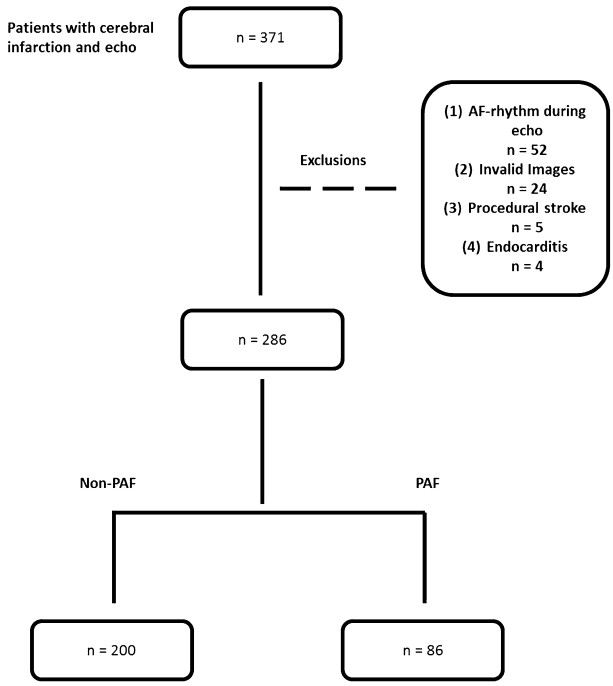

Figure 1. *Flowchart depicting the inclusion, exclusion, and distribution of the study population. Abbreviations: AF, atrial fibrillation; echo, echocardiography; PAF, paroxysmal atrial fibrillation.*

The remaining population (n = 286) was divided according to AF, resulting in a PAF group (n = 86) and a non-PAF group (n = 200). PAF was considered present when reported at least once, and when occurring either before and/or after the index stroke. Incidence of AF was evaluated by reviewing electronic medical files. These were supplemented with the reporting notes from the echocardiograms. The same approach was used for assessment of medical history and clinical baseline values.

Echocardiograms

All echocardiograms were stored digitally using an Image Vault (GE Vingmed Ultrasound AS, Horten, Norway) and were analyzed offline with commercially available software (EchoPac, BT12, GE Vingmed Ultrasound AS, Horten, Norway) by a single investigator who was blinded to all other patient data. All measurements were performed on a single heart cycle.

Conventional Echocardiography

Interventricular septal wall thickness, left posterior wall thickness, and left ventricular internal diameter were measured at end diastole in the parasternal longitudinal axis projection. The left ventricular ejection fraction (LVEF) was calculated by the modified Simpson's biplane method.