

Prevalence and predictors of silent atrial fibrillation in high risk patients detected by prolonged continuous Holter monitoring

Atrial fibrillation (AF) is becoming epidemic, affecting 1% to 1.5% of the population in the developed world. Projected data from the population-based studies suggest that the prevalence of AF will grow at least 3-fold in the next 4 decades. It has been estimated that 2.5-3% of the population will be affected by AF by 2050. Most who suffer from the arrhythmia are over 70 years of age, with a prevalence of 9.1% for men and 4.7% for women aged 65-84 years in the Framingham Study. AF is classically associated with hypertension, heart failure, myocardial infarction, mitral stenosis, thyrotoxicosis, and alcohol. Moreover, also left atrium dilation detected by transthoracic echocardiogram (TTE) is associated with an increased risk of AF, with a 40% excess risk of AF for a 5 mm increase in left atrial size. The most significant risk related with AF is arterial thrombo-embolism and stroke. Embolism of cardiac origin accounts for about one fifth of ischaemic strokes. Strokes in AF are typically more severe, are associated with greater disability, and are prone to early recurrence. Both persistent AF and paroxysmal AF are potent predictors of first and recurrent stroke.

Multiple clinical trials have demonstrated the superior therapeutic effect of oral anticoagulation compared with placebo in the prevention of thromboembolic events among patients with nonvalvular AF. New oral anticoagulant drugs that may not need monitoring are on the horizon.

Diagnosis of AF on routine electrocardiogram is straightforward when the arrhythmia is persistent or permanent. Paroxysmal atrial fibrillation, however, has been reported to be asymptomatic in up to 50% of patients and can therefore be difficult to detect. In some cases, asymptomatic AF is revealed only after complications, such as stroke or congestive heart failure have occurred.

As the risk of AF-related complications is not different between short AF episodes and sustained form of arrhythmia, it is important to detect paroxysmal AF, in order to prevent AF-related complication (e.g. stroke). However, data of the real prevalence of silent AF are scarce, and the proper diagnostic test for its diagnosis has not been established, yet.

AIM

The aim of the present study is to assess feasibility and detection rates of AF with continuous 7-day Holter monitoring applied in patients at risk for AF, who may benefit from oral anticoagulant if a diagnosis of AF is provided.

METHODS

This is a two-Centers, prospective feasibility pilot trial. All patients presenting to the Ambulatories of the Cardiology Department of Ospedali Riuniti di Bergamo or Clinica San Francesco for outpatient visits or echocardiograms and in-hospital patients admitted to the Cardiology ward will be analyzed. Inclusion criteria are age ≥ 65 years, left atrium dilation, and the presence of at least one of the following clinical risk factors: hypertension with left ventricular hypertrophy, heart failure with left ventricular ejection fraction $\leq 35\%$, previous myocardial infarction with left ventricular ejection fraction $\leq 35\%$, or mitral stenosis.

Exclusion criteria are history of AF, detection AF at basal ECG, and previous stroke or transient cerebral ischemic attack. All patients with at least 1 of the clinical aforementioned risk factors will be asked to give preliminary consent for participation to allow for TTE.

Patients with left atrium dilation at TTE will be included in the study. A basal ECG will be performed to all patients before applying 7-days Holter monitoring. The study will be stopped after the enrollment of 200 patients.

Definitions

Heart failure and myocardial infarction are defined according to the International Guidelines. Left ventricular ejection fraction will be assessed at TTE, using the biplane Simpson's method.

Left ventricular hypertrophy is defined as left ventricular mass > 108 g/mq for women and > 131 mg/mq for men, detected at TTE.

Mitral valvular stenosis is defined as mitral valve area $< 1,5$ cmq, detected at TTE.

Left atrium dilation is defined as left atrium indexed volume > 33 ml/mq, detected at TTE.

Presence of AF will be defined as at least 1 period of > 30 seconds' duration of an absolute arrhythmia without detectable P waves and without a pattern more consistent with an alternative diagnosis. To add detail, we will also calculate overall detection rates for shorter (> 10 supraventricular ectopic complexes in a row) as well as longer (> 5 continuous hours) periods of atrial fibrillation. Detected episodes will be verified by a specialist in

electrophysiology blinded to clinical data. Detection rates will be calculated as a fraction of all patients who had received 7-day Holter monitoring (including those with inadequate quality of recordings).

Data collection and clinical examination

Baseline characteristics will be recorded by a standardized questionnaire, including a detailed medical history and baseline medication. Electrocardiographic recordings will be analyzed offline by 2 investigators blinded to clinical data of the patients using dedicated analysis software. Day 4 of the recording will be defined as a 24-hour period that would have been recorded as part of standard care. The recordings will be analyzed with a focus on the detection of AF. Briefly, heart rate and RR variability plots will be checked for patterns suggestive of AF, >20 electrocardiographic strips representing fastest and slowest heart rates will be inspected and arrhythmias, and supraventricular tachycardias and supraventricular premature complexes as detected by the automated software algorithm will be scanned. In cases of low-quality recordings, we will deviate from this algorithm to more intensive analyses up to manual review of the whole recording period.

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