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Atrial fibrillation and long-term prognosis of patients with stable coronary heart disease: Relevance of routine electrocardiogram

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Atrial fibrillation (AF) is an emerging public health issue given the increasing prevalence, associated morbidity, and health care costs, yet the long-term prognostic value of AF has not been well characterized after acute coronary syndromes (ACS). This study evaluated the association of AF prevalence at baseline as identified by routine electrocardiogram (ECG) with the onset of fatal- and non-fatal adverse cardiovascular events (CVE) over a 13-year follow-up among patients with coronary heart disease (CHD).

We conducted a prospective cohort study in patients with incident CHD aged 30–70 years from two in-patient rehabilitation centers in Germany between January 1999 and May 2000 [1]. All participants gave written informed consent and Ethics Boards approved the study. All patients underwent a routine standard 12-lead ECG at the beginning of rehabilitation. A trained investigator defined AF according to a standardized protocol.

Follow-up was conducted one, three, four and a half, six, eight, ten, and thirteen years after rehabilitation. CVE information was obtained from primary care physicians and death certificates were obtained from local public health departments. CVE were defined as CHD

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The authors declared no conflict of interest.

as the underlying cause of death, non-fatal myocardial infarction (MI), or ischemic cerebrovascular event (transient ischemic attack or stroke). Of the 1182 participants with available ECGs, we excluded those not in sinus rhythm for reasons other than AF (n = 14), no follow-up (n = 87), or missing CHD severity (n = 53), leaving 1028 patients for analysis.

We used a Cox proportional hazards model to estimate the association of AF with CVE during follow-up. We formed a parsimonious model by including potential confounders if they were significant predictors of adverse CVE ($p < 0.10$) or if their inclusion changed the AF parameter estimate by $> 10\%$.

There were 27 patients with incident persistent AF (2.6%) and 1001 patients in sinus rhythm at baseline. The prevalence of AF among age groups was 0% for 30 to 39, 0.8% for 40 to 49, 1.3% for 50 to 59, and 3.8% for 60 to 70 years old. Those with AF were on average older, had a higher body mass index, higher heart rate, more severe CHD, more frequent history of diabetes, and use of ACE inhibitors (Table 1). Over 13 years, 252 subsequent CVE occurred (median time to event = 7.2 years; 37.7% cerebrovascular). Patients with AF had a 2.4 (95% confidence interval (CI): 1.4 to 3.9) higher risk for adverse CVE compared with patients in sinus rhythm in the fully adjusted model (Table 2).

In a population of stable CHD patients, the prevalence of AF as determined by a routine resting ECG at baseline, probably mostly permanent AF, was 2.6% overall, with a maximum of 3.8% in the 60 to 70 year olds. AF was independently associated with over a 2-fold risk of a CVE compared with those in sinus rhythm during long-term follow-up. AF has been associated with one-year mortality and 30-day risk of stroke among ACS patients [2] and one-year mortality among patients admitted to a coronary care unit in Sweden [3]. The prevalence of AF in these studies was 6% [2] and 15%, [3] respectively, which is higher than in the current study and could be partially explained by the older age of patients and multiple ECG measurements.

Using a composite endpoint similar to our study, a study among a registry of ACS patients showed a one-year risk of a composite endpoint (all deaths, MI and stroke) of 1.66 (95% CI: 1.18 to 2.33) for new-onset AF and 1.13 (95% CI: 0.86 to 1.49) for preexisting AF compared with patients without AF [4]. We did not have previous history of AF, but in line with our long-term data, AF was associated with worse prognosis regardless of prior history; although evidence suggests new-onset AF carries a higher risk.

AF might be underestimated in our study since we used one standard, resting ECG and most likely detected permanent than paroxysmal AF. Currently, there is no consensus on the optimal method to detect AF. Longer recording periods through 24 h Holter monitoring or implantation of a loop-recorder would increase the likelihood of detecting AF. A randomized, controlled trial among patients with cryptogenic stroke showed that those who received an insertable cardiac monitor had better AF detection by 6 months at 8.9% compared with those who received standard care at 1.4% [5]. Given the associated risk and preventive treatment approaches of AF, our results indicate that opportunistic screening should be incorporated into regular physician visits of CHD patients. Further limitations of

this study include residual confounding, and potentially imprecise estimates given the small number of patients with AF.

We found that AF was a marker of poor prognosis over 13 years, which has major implications for secondary prevention and management of AF, especially since these high-risk patients could be identified by one routine ECG. Further research is needed to determine how systematic ECG monitoring to identify AF could be integrated into effective management strategies in patients with CHD.

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Table 1

Sociodemographic and medical characteristics by atrial fibrillation status among patients with stable coronary heart disease.

Variable	<u>In sinus rhythm (N = 1001)</u>	<u>Atrial fibrillation (N = 27)</u>
	N (%) or mean $\pm$ SD	N (%) or mean $\pm$ SD
Women, n (%)	152 (15.2)	5 (18.5)
Age (years), mean $\pm$ SD	58.9 $\pm$ 8.0	63.5 $\pm$ 5.5
BMI (Kg/m ²), mean $\pm$ SD	26.9 $\pm$ 3.3	27.9 $\pm$ 3.5
Heart rate (bpm), mean $\pm$ SD	72.5 $\pm$ 14.1	90.3 $\pm$ 20.4
Smoking status, n (%)		
Current	46 (4.6)	1 (3.7)
Former	633 (63.2)	16 (59.3)
Never	322 (32.2)	10 (37.0)
History of myocardial infarction, ^a n (%)	584(58.3)	18 (66.7)
Coronary heart disease severity, number of affected vessels, n (%)		
0/1	275 (27.5)	7 (25.9)
2	280 (28.0)	5 (18.5)
3	446 (44.6)	15 (55.6)
History of diabetes mellitus, n (%)	168 (16.8)	7 (25.9)
Angiotensin-converting enzyme inhibitor, n (%)	524 (52.5)	21 (77.8)
Aspirin, n (%)	881 (88.3)	13 (48.1)
Clopidogrel or Ticlopedin, n (%)	92 (9.2)	0 (0)

SD, standard deviation.

^aReason for last stay in hospital before rehabilitation.

Table 2

Risk of fatal and non-fatal cardiovascular disease events (CVE) during the 13-year follow-up according to atrial fibrillation status among patients with stable coronary heart disease.

Variable	In sinus rhythm (N = 1001)	Atrial fibrillation (N = 27)
Follow-up time (years), median (interquartile range)	12.1 (6.6–13.0)	9.6 (5.3–12.6)
Fatal and non-fatal CVE, n	235	17
Rate of CVE/1000 patient-years (95% CI)	24.3 (21.2–27.4)	71.2 (37.4–105.1)
<i>Risk of CVE associated with atrial fibrillation, hazard ratio (95% CI)</i>		
Model 1, adjusted for age, gender and center	1 (reference)	2.6 (1.6–4.3)
Model 2, fully adjusted ^a	1 (reference)	2.4 (1.4–3.9)

CVE, cardiovascular disease events; CI, confidence interval.

^aThe following potential confounders at baseline were considered in multivariable analyses: heart rate, body mass index, HDL cholesterol, LDL cholesterol, **smoking status (current, former, never)**, **history of myocardial infarction**, history of heart failure, **history of diabetes mellitus**, **coronary heart disease severity (number of affected vessels by angiographic score)**, and discharge prescription at baseline for β -blockers, **angiotensin-converting enzyme inhibitors**, calcium channel blockers, lipid-lowering drugs, or aspirin (bold ones were included in final model as they were significant predictors of adverse CVE ($p < 0.10$) or their inclusion changed the atrial fibrillation parameter estimate by $> 10\%$).