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Abbreviations
AF: Atrial fibrillation
CAD: Coronary artery disease
CI: Confidence interval
IRR: Incidence rate ratios
TIA: Transient ischemic attack

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Patients with atrial fibrillation (AF) have an increased risk of ischemic stroke, transient ischemic attack (TIA), and systemic embolism compared to patients without AF (1). In patients with AF, several risk factors are well documented and included in risk scores used for risk stratification. These include advancing age, diabetes mellitus, hypertension, congestive heart disease, peripheral artery disease, and previous stroke/TIA, among others. Coronary artery disease (CAD) and ischemic stroke share several common risk factors, but whether CAD is an independent risk factor for ischemic stroke among patients with AF has not yet been examined. The aim of this study was to investigate whether the presence of CAD provided independent prognostic information of the risk of future ischemic stroke and thromboembolism in patients with AF.

The association between CAD and ischemic stroke risk was examined in a large prospectively collected dataset of consecutive patients with AF who underwent coronary angiography in Western Denmark between July 1, 2004 and December 1, 2012. All patients' angiographic findings are registered in the Western Denmark Heart Registry (2) by use of each patient's unique 10-digit personal identifier, which is a personal number assigned to each Danish resident upon birth or after immigration. This personal identifier is used throughout every regional and national registry, where it ensures accurate cross linkage of healthcare information and minimizes loss to follow-up. Patient data from the Western Denmark Heart Registry concerning the patients' angiographic findings were cross linked with information from the Danish National Patient Registry,(3) which records all hospital-based inpatient and outpatient diagnoses, and the Danish National Database of Reimbursed Prescriptions (3), which contains data on all reimbursed prescriptions at Danish pharmacies.

The total study cohort was divided into two groups; patients with CAD and patients without CAD. CAD was defined as obstructive (≥50%) coronary stenosis in ≥1 coronary vessel, or non-obstructive coronary stenoses in ≥2 coronary vessels. The primary endpoint was a composite of ischemic stroke, TIA, and systemic embolism obtained from the Danish National Patient Registry. Follow-up began 30 days after the index coronary angiography, and continued until endpoint event, death, emigration, or end of follow-up, whichever came first. The risk of ischemic stroke, TIA, and systemic embolism was estimated separately for both groups, and incidence rate ratios (IRR) were calculated with modified Poisson regression using patients without CAD as reference. We adjusted for age, gender, diabetes mellitus, hypertension, congestive heart disease, previous stroke/TIA, vascular disease (previous myocardial infarction and/or peripheral artery disease/aortic plaque), antiplatelet treatment, oral anticoagulant treatment, and statin treatment.

Out of 96,430 patients undergoing coronary angiography between 2004-2012, a total of 12,690 patients had a diagnosis of AF, were 18 years or above and had a follow-up time of >30 days. Among these patients 7,533 patients (59.4%) had CAD and 5,157 patients (40.6%) had no CAD. Maximal follow-up was 8.4 years, and median follow-up was 3 years (IQR 1.3-5.2). Baseline characteristics are shown in Table 1. The rate of ischemic stroke/TIA/thromboembolism was 2.62 (95% confidence interval (CI) 2.42-2.84) per 100 person-years for patients with CAD and 1.61 (95% CI 1.43-1.81) per 100 person-years for patients without CAD. Crude IRR was 1.62 (95% CI 1.41-1.87). The impact of presence of CAD remained significant after adjustment and suggested a 29% increased risk of ischemic stroke/TIA/thromboembolism (adjusted IRR 1.29, 95% CI 1.08-1.53).

Our study suggests that CAD is an independent risk factor for ischemic stroke among patients with AF. The association between CAD and ischemic stroke has also been indicated in a previous study analyzing our entire cohort, i.e. primarily including patients without AF.(3) Patients with AF, however, have a greater risk of ischemic stroke than patients without AF. Moreover, prophylactic oral anticoagulant therapy is well-documented in patients with AF but not in non-AF patients. There are several risk scores recommended for risk stratification of AF patients into those with a low risk of thromboembolic events (no indication for oral anticoagulation) and those with a high risk (indication for oral anticoagulation) of thromboembolic events including ischemic stroke. According to the current study, CAD is an independent risk factor for thromboembolic events including ischemic stroke in AF patients. Consequently, we suggest that CAD should be considered as a potential additional risk factor in the risk scores used for stratification of AF patients.

References

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Table 1. Baseline characteristics of 12,690 patients with atrial fibrillation undergoing coronary angiography

	No CAD[*] (n=5,157) n (%)	Any CAD (n=7,533) n (%)	Total (n=12,690) n (%)
Age			
<65 years	2,050 (39.8)	1,478 (19.6)	3,528 (27.8)
65-74 years	1,764 (34.2)	2,801 (37.2)	4,565 (36.0)
≥75 years	1,343 (26.0)	3,254 (43.2)	4,597 (36.2)
Gender			
Male	3,081 (59.7)	5,363 (71.2)	8,444 (66.5)
Female	2,076 (40.3)	2,170 (28.8)	4,246 (33.5)
Smoking status			
Never/former	3,632 (70.4)	5,105 (67.8)	8,737 (68.8)
Active	835 (16.2)	1,501 (19.9)	2,336 (18.4)
Missing	690 (13.4)	927 (12.3)	1,617 (12.7)
Comorbidities			
Diabetes mellitus	735 (14.3)	1,664 (22.1)	2,399 (18.9)
Hypertension	3,033 (58.8)	5,420 (72.0)	8,453 (66.6)
Congestive heart failure	1,933 (37.5)	2,991 (39.7)	4,924 (38.8)
Stroke/TIA[†]	564 (10.9)	1,116 (14.8)	1,680 (13.2)
Vascular disease[‡]	733 (15.0)	3,752 (49.8)	4,525 (35.7)
PAD[§]/aortic plaque	282 (5.5)	1,087 (14.4)	1,369 (10.8)
Previous myocardial infarction	536 (10.4)	3,171 (42.1)	3,707 (29.2)
Medical treatment			
Vitamin K antagonists	3,390 (65.7)	4,125 (54.8)	7,515 (59.2)
NOAC[//]	97 (1.9)	119 (1.6)	216 (1.7)
Aspirin	2,608 (50.6)	5,919 (78.6)	8,527 (67.2)
Statin	2,226 (43.2)	5,915 (78.5)	8,141 (64.2)

[*] CAD: Coronary artery disease

[†] TIA: Transient ischemic attack

[‡] Vascular disease: Presence of previous myocardial infarction and/or peripheral artery disease/aortic plaque.

[§] PAD: Peripheral artery disease

[//] NOAC: Non-vitamin K antagonist anticoagulant treatment