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Previous history of hyperthyroidism in emergency department patients with atrial fibrillation does not increase the risk of thromboembolism and death

Dear Editor,

Atrial fibrillation (AF) is frequently encountered in the emergency department (ED) and is a major risk factor for thromboembolic events. The clinical decision for anticoagulation is guided by risk scoring systems that include factors such as age, sex and comorbidities.[1,2] AF can sometimes occur in patients with active hyperthyroidism, but because the condition is often transient and reversible, most risk scores and guidelines do not recommend anticoagulation for these patients.[3-7] However, few studies have evaluated if a past history of hyperthyroidism affects stroke rates in patients with AF. We review the data collected from a large international AF registry to study this relationship.

The Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY)-AF registry prospectively collected data of patients presenting to the ED (or equivalent acute care setting) of participating sites with AF as the primary or secondary diagnosis.[8,9] Information regarding demographics, past medical history and medications was collected, and a 1-year follow-up regarding outcomes of death and thromboembolic events was done with written consent from the patients. This included a history of hyperthyroidism. A total of 15,400 patients were recruited from 2008 to 2011 at 164 sites in 46 countries. The study design and protocol were developed by the principal investigators of the original trial, and the study was coordinated and data were managed by the Population Health Research Institute at McMaster University in Hamilton, Canada, with assistance from regional coordination centres.

Baseline demographic information, and anticoagulation, antiplatelet and rate control strategies were summarised for patients with and without a past history of hyperthyroidism. Data were collected through interviews with patients, review of medical records, and contacts with treating physicians.

A past history of hyperthyroidism was reported in 571 (3.7%) of all recruited patients. The prevalence of a prior history of hyperthyroidism was highest in those from Eastern Europe at 7.0%, followed by Southeast Asia at 5.4%. Patients with a history of hyperthyroidism were more likely to be female (64.4% versus 46.5%, $P<0.001$) and have a history of prior AF (72.9% vs 64.3%, $P<0.001$). They were less likely to have a history of rheumatic heart disease (6.3% vs 11.8%, $P<0.001$), significant valvular disease as defined by moderate-to-severe or severe regurgitation or stenosis on echocardiography (14.4% vs 22.0%, $P<0.001$), and history of myocardial infarction (11.4% vs 14.5, $P=0.037$) compared with patients without history of hyperthyroidism. They also did not appear to have an increased risk of stroke or transient ischaemic attack prior to involvement in the study (13.1% vs 13.8%, $P=0.633$). There was no difference in the $CHADS_2$ (congestive heart failure, hypertension, age≥75 years, diabetes mellitus, stroke) score or congestive heart failure, hypertension, age >75 years, diabetes, and stroke/transient ischaemic attack, and vascular disease, age 65–74 years (CHA_2DS_2-VASc) scores between patients with and without history of hyperthyroidism (Table 1).

Permanent AF was the predominant subtype in both groups (37.7% in those with prior history of hyperthyroidism and 40.5% in those without, $P=0.181$), followed by paroxysmal and then persistent AF. This differs from other large registries such as the ORBIT-AF (Outcomes Registry for Better Informed Treatment of Atrial Fibrillation) registry that reports about half the patients have paroxysmal AF.[10] It is probable that the ED setting might have selected more clinically advance disease, i.e. more permanent than paroxysmal AF, compared with other registries that recruited from more diverse sources.

Patients with a previous history of hyperthyroidism were more likely to receive beta-blockers compared to those without this history (56.6% vs 48.8%, $P<0.001$). Aspirin use was lower at the 1-year follow-up in patients with a history of prior hyperthyroidism compared with those without (37.6% vs 41.8%, $P=0.047$). There was no difference between the 2 groups for oral anticoagulant use (45.7% for those with a past history vs 42.0% for those without, $P=0.079$). After multivariable adjustment, there was no difference between patients with and without a history of hyperthyroidism in terms of rates of overall death (odds ratio [OR] 0.93, confidence interval [CI] 0.65–1.34, $P=0.664$), cardiovascular death (OR 1.18, CI 0.75–1.86, $P=0.413$), and stroke/non-central nervous system (CNS) embolism (OR 0.76, CI 0.44–1.30, $P=0.267$) at the end of 1 year. There was also no difference in the rate of recurrent AF (OR 1.18, CI 0.92–1.50, $P=0.158$) after 1 year (Table 1).

Table 1. Baseline charateristics, and anticoagulation and rate control strategies at 1 year

	Prior history of hyperthyroidism	No prior history of hyperthyroidism	*P* value[a]
Baseline characteristics	**n=571**	**n=14829**	
Age, mean±SD, years	65.8±13.9	65.9±14.8	0.887
Male, no. (%)	203 (35.6)	7928 (53.5)	<0.001
Smoker, no. (%)	89 (15.6)	2522 (17.0)	0.375
History of diabetes mellitus, no. (%)	121 (21.2)	3242 (21.9)	0.703
History of hypertension, no. (%)	362 (63.4)	9189 (62.0)	0.489
History of heart failure, no. (%)	201 (35.2)	5147 (34.7)	0.808
History of CAD, no. (%)	179 (31.3)	4837 (32.6)	0.525
History of MI, no. (%)	65 (11.4)	2150 (14.5)	0.037
History of rheumatic heart disease, no. (%)	36 (6.3)	1752 (11.8)	<0.001
History of stroke or TIA, no. (%)	75 (13.1)	2052 (13.8)	0.633
Significant valvular heart disease, no. (%)	82 (14.4)	3267 (22.0)	<0.001
Prior diagnosis of AF before visit, no. (%)	416 (72.9)	9533 (64.3)	<0.001
Type of AF at ED visit			
Persistent, no. (%)	149 (26.1)	3763 (25.4)	0.699
Paroxysmal, no. (%)	207 (36.3)	5060 (34.1)	0.292
Permanent, no. (%)	215 (37.7)	5999 (40.5)	0.181
AF/flutter when patients left ED, no. (%)	433 (75.8)	11681 (78.8)	0.092
Lone AF, no. (%)	0 (0)	796 (5.4)	<0.001
$CHADS_2$ score, median (IQR)	2.0 (1.0–3.0)	2.0 (1.0–3.0)	0.874
CHA_2DS_2-VASc score, median (IQR)	3.0 (2.0–5.0)	3.0 (2.0–5.0)	0.170
Beta blocker prior to ED visit, no. (%)	286 (50.1)	6150 (41.5)	<0.001
Beta blocker after ED visit, no. (%)	378 (66.2)	8021 (54.1)	<0.001
Anticoagulation and rate control strategies at 1 year visit	**n= 569**	**n=14792**	
Received ASA, no. (%)	214 (37.6)	6182 (41.8)	0.047
Received OAC, no. (%)	260 (45.7)	6211 (42.0)	0.079
Received anti-arrhythmic drug, no. (%)	117 (20.6)	3255 (22.0)	0.415
Received rate control drug, no. (%)	419 (73.6)	10390 (70.2)	0.082
Calcium channel blockers, no. (%)	90 (15.8)	2242 (15.2)	0.667
Beta blockers, no. (%)	322 (56.6)	7216 (48.8)	<0.001
Digoxin, no. (%)	139 (24.4)	4017 (27.2)	0.151
Received cardioversion, no. (%)	52 (9.1)	1170 (7.9)	0.288
Received AV node ablation, no. (%)	6 (1.1)	75 (0.5)	0.126
Received AF ablation, no. (%)	13 (2.3)	349 (2.4)	0.908

AF: atrial fibrillation; ASA: acetylsalicylic acid (aspirin); AV: atrioventricular; CAD: coronary artery disease; $CHADS_2$: congestive heart failure, hypertension, age>75 years, diabetes mellitus, stroke; CHA_2DS_2-VASc: congestive heart failure, hypertension, age >75 years, diabetes, and stroke/transient ischaemic attack, and vascular disease, age 65–74 years; ED: emergency department; IQR: interquartile range; MI: myocardial infarction; OAC: oral anticoagulant; SD: standard deviation; TIA: transient ischaemic attack

[a] *P* value is from chi-square test for categorical variables, two-sample t-test for normally distributed variables, and Wilcoxon rank-sum test for non-normally distributed variables.

This large multinational registry demonstrates that a prior history of hyperthyroidism does not appear to be an independent risk factor for 1-year risk of overall death, cardiovascular death, stroke/non-CNS thromboembolism and recurrent AF in patients with AF. The strength of this study lies in the extensive, international multicentre records of the AF RE-LY registry, and the subsequent follow-up that captured outcomes and details of anticoagulation and rate control strategies.

The clinical implication of our study is that a history of prior hyperthyroidism does not appear to impact the risk of AF complications. Thus, for patients with a history of hyperthyroidism, the use of oral anticoagulation should continue to be selected according to the CHA_2DS_2-VASc score.

As this study was retrospectively performed, thyroid function test results and details of treatment of hyperthyroidism were not collected at baseline or at the follow-up visit, and neither was the information on AF onset in relation to the diagnosis of hyperthyroidism. Patients with a past history of hyperthyroidism were more likely to receive beta-blockers for their AF. It was possible that some of these patients had active hyperthyroidism at their ED visit but because no data were collected about their thyroid status, we have no way of ascertaining it. Future studies looking at AF in patients in the ED should consider including information on thyroid status during index visit and follow-up.

In summary, nearly 1 in 25 patients presenting to the ED with AF have prior history of hyperthyroidism. The latter is not an independent risk factor for thromboembolic complications and death, and should not influence therapeutic decisions for anticoagulation.

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