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Atrial fibrillation and use of antithrombotic medications in older people: A population-based study☆

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ABSTRACT

Background: Trends in the use of antithrombotic drugs in elderly patients with atrial fibrillation (AF) are largely unknown. We estimated the prevalence of AF in an older population, and examined whether use of anticoagulant and antiplatelet drugs in older AF patients has changed over time.
Methods: Data from the population-based Swedish National study on Aging and Care in Kungsholmen ($n = 3363$, age ≥ 60 years, 64.9% women) were used (2001–2004 and 2007–2010). AF cases were identified through 12-lead electrocardiogram, physician examinations, and patient register records (ICD-10 code I48). We used the $CHADS_2$ and CHA_2DS_2-VASc scores to estimate stroke risk, and an incomplete HAS-BLED score to estimate bleeding risk.
Results: At baseline (2001–2004), 328 persons (9.8%) were ascertained to have AF. The prevalence of AF increased significantly with age from 2.8% in people aged 60–66 years to 21.2% in those ≥90 years, and was more common in men than in women (11.2% vs. 9.0%). Among AF patients with $CHADS_2$ score ≥2 at baseline, 25% were taking anticoagulant drugs and 54% were taking antiplatelet drugs. High bleeding risk was significantly associated with not using anticoagulant drugs in AF patients (multi-adjusted OR = 2.50, $p = 0.015$). Between 2001–2004 and 2007–2010, use of anticoagulant drugs increased significantly, especially in AF patients with CHA_2DS_2-VASc score ≥2 (23% vs. 33%, $p = 0.008$) and in those with HAS-BLED score <3 (32% vs. 53%, $p = 0.004$).
Conclusion: AF is common among old people. The use of anticoagulant drugs increased over time in AF patients, yet still two-thirds of those with high stroke risk remained untreated.

1. Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, with a lifetime risk of ~25% in people over 40 years of age [1]. It is well-established that AF increases the risk of stroke, heart failure, and hospitalization [2–4]. With population aging, AF is becoming a major public health issue worldwide and is likely to exert greater burden on the healthcare system in the years to come [2].

AF-related thromboembolism can be largely prevented by appropriate antithrombotic treatments. Meta-analyses have shown that anticoagulant drugs can reduce the risk of stroke by 64% and risk of death by 26% in AF patients [5]. Consensus guidelines have proposed the use of risk scoring systems, such as $CHADS_2$ and CHA_2DS_2-VASc scores, to estimate stroke risk in AF patients. These guidelines recommend the initiation of anticoagulation in those who are at intermediate or high risk of stroke [6], while the use of antiplatelets as an alternative to anticoagulant drugs should be minimized [7]. Bleeding risk, measured by the recently developed tool HAS-BLED score [8], should also be part of the evaluation although a high bleeding risk should call for regular review of the patients rather than withdrawal of anticoagulation [7]. In the real world setting, however, anticoagulant treatment often falls short of guideline-based expectations in both developed and developing countries [9,10], driven largely by concerns of major bleeding [11,12]. Several hospital-based studies have implied a slight increase in the prescription of anticoagulants over time [13–15], but the temporal change in the use of antithrombotic medications while taking into account both stroke and bleeding risk schemes has been scarcely investigated among AF patients in the general older population.

The Swedish National Study on Aging and Care in Kungsholmen (SNAC-K) is a large population-based longitudinal study of elderly people. By using the SNAC-K database, we aimed to 1) estimate the prevalence of AF in people aged ≥60 years; and 2) examine whether

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use of antithrombotic drugs in people with AF has changed over a 6-year period, taking into account both stroke and bleeding risk.

2. Methods

2.1. Study population

We used data from the SNAC-K, which consists of a sample of people aged 60 years and above living at home or in institutions in the Kungsholmen district, an area of central Stockholm. The target population was stratified into eleven age groups with different intervals: six years in younger cohorts (60, 66, and 72 years) and three years in older cohorts (78, 81, 84, 87, 90, 93, 96, and ≥99 years), after which a random sample was drawn from each of these age groups [16]. Of all the 5111 people invited, 4590 were alive and eligible, and 3363 (73.3%) attended the baseline interview. Participants received baseline examination between 2001 and 2004, and were followed up after six years for the younger age cohorts (60–72 years, re-examined 2007–2010) and every three years for the older age cohorts (78 years and above, re-examined 2004–2007 and 2007–2010). A new random sample of people aged 81 years ($n = 194$) was recruited from the same area and examined during 2007–2010.

All parts of SNAC-K (including linkage with patient registers) were approved by the Regional Ethical Review Board in Stockholm. Written informed consent was obtained from all participants or, in case of cognitively impaired persons, from proxies.

2.2. Data collection and assessments

Data at baseline and each follow-up were collected through face-to-face interviews, clinical examinations, and laboratory tests following standard procedures [16]. During the study visit, a comprehensive review of the participants' health conditions and history of diseases was conducted by the physicians based on clinical examinations, medical charts, and self-reports. Diseases identified by the examining physician were recorded with ICD-10 codes (International Classification of Diseases, Tenth Revision). The Swedish national inpatient register and Stockholm county inpatient and outpatient registers were also linked to the SNAC-K database; register records (ICD-10 codes) before the date of each examination were used to identify diseases at each phase. In brief, we collected data on demographic factors (age, sex, and education), lifestyle factors (e.g. alcohol drinking), health conditions (e.g. AF, heart failure, hypertension, diabetes), and use of medications classified according to the Anatomical Therapeutic Chemical (ATC) Classification System. *Education* was assessed as total years of formal schooling, and categorized into elementary school (<8 years) and above elementary school (≥8 years). *Problem drinking* was defined as having a score ≥8 using the Alcohol Use Disorders Identification Test (AUDIT) questionnaire at each study examination. *Smoking* was categorized as never/former and current smoking. *Physical activity* was divided into inactive (light and/or intensive exercise ≤2–3 times per month) and moderate/intensive (light, moderate, or intensive exercise several times per week). *Obesity* was defined as having a body mass index (BMI) ≥30 kg/m^2. *Dementia* was diagnosed according to the Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition (DSM-IV) criteria by physicians.

We identified AF cases based on electro-cardiogram (ECG) conducted during study visit and ICD-10 codes (I48) from physician's diagnosis or register records. The following chronic morbidities were identified from the combination of physician's diagnosis and register records: *heart failure* (*HF*) (ICD-10 codes: I110, I130, I132, I27, I280, I42, I43, I50, I515, I517, I528, Z941, and Z943), *ischemic stroke/transient ischemic attack* (*TIA*) (G45, I63-I64, and I74), *myocardial infarction* (I21 and I22), *peripheral diseases* (I73, I792, I798, I702, I731, and I738), *abnormal liver function* (K70–K77), and *major bleeding* including both intracranial and gastrointestinal bleeding (I60–I62, I850, I983, K26–K28, K625, K922, and D62) [17]. *Hypertension* was defined as blood pressure ≥140/90 mmHg or current use of antihypertensive agents (ATC codes C02, C03, C07, C08 and C09). *Coronary heart disease (CHD)* was defined as having a diagnosis from the physicians or register records (ICD-10 codes I20–22, I24–25, Z951, and Z955), or use of nitrates (ATC code C01DA) or ranolazine (C01EB18). *Diabetes* was defined as having a self-reported history of diabetes, records of diabetes from the register (ICD-10 codes E10-E14), use of diabetes drugs (ATC code A10), or having HbA1c >6.4%. *High cholesterol* was defined as having non-fasting total serum cholesterol ≥6.22 mmol/L or use of lipid-lowering drugs (ATC code C10). *Abnormal renal function* was defined as having a diagnosis from the physicians or register records (ICD 10 codes: N17–N19, I12, and I13), or having an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2, which was calculated based on the serum creatinine level using the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) formula [18].

Antithrombotic treatment included the use of anticoagulant drugs (ATC code B01AA) and antiplatelet drugs (B01AC).

2.3. Assessment of stroke and bleeding risk

We characterized the study participants by using three scoring systems to estimate thromboembolic risk and bleeding risk in people with AF. We used the traditional $CHADS_2$ score (1 point each for heart failure, hypertension, age ≥ 75 years, and diabetes and 2 points for ischemic stroke/TIA) and the more recently developed CHA_2DS_2-VASc score (1 point each for heart failure, hypertension, diabetes, vascular diseases including peripheral arterial diseases and myocardial infarction, age 65–74, and female sex, and 2 points each for age ≥75 years and ischemic stroke/TIA) to estimate thromboembolic risk [6]. For both $CHADS_2$ and CHA_2DS_2-VASc, a score ≥2 indicates high risk of thromboembolism. The HAS-BLED score was used to measure the bleeding risk in our study. However, since our dataset did not contain labile INR, we calculated an incomplete HAS-BLED score in AF patients (1 point each for hypertension, abnormal renal function, abnormal liver function, ischemic stroke/TIA, major bleeding, and age ≥65 years, and 1 or 2 points for drug/alcohol use). A HAS-BLED score ≥3 indicates high risk of major bleeding [6]. Drug/alcohol use refers to the concomitant presence of problem drinking and drug use including anti-platelet agents (ATC code: B01AC) and nonsteroidal anti-inflammatory drugs (M01A and N02BA).

2.4. Statistical analysis

Characteristics in people with and without AF were compared using chi-square tests for categorical variables and *t*-tests for continuous variables. The crude prevalence of AF by age and sex was calculated at baseline, and was standardized to the age and sex structure of Swedish national population between 2001 and 2004, where the age groups corresponding to that of SNAC-K were used. Proportions of antithrombotic drug use at baseline among participants with AF were calculated; AF patients who had missing information on medication use were excluded in this analysis ($n = 1$). Logistic regressions were performed to assess the association between not being treated with anticoagulant drugs and bleeding risk in AF patients at baseline, adjusting for age, sex, education, obesity, smoking, physical activity, diabetes, high cholesterol, heart failure, vascular diseases, and dementia. The analytical sample for the comparison of use of antithrombotic drugs between baseline (2001–2004) and 6-year follow-up (2007–2010) included participants with AF aged over 66 years. Logistic regressions were used to compare the proportion of antithrombotic drug use in AF between baseline and 6 years later, adjusting for age, sex, and education. The significance level was set at 0.05. We used Stata version 13 (StataCorp, TX, USA) for all analyses.