Atrial fibrillation patients at intermediate risk of stroke rapidly progress to high stroke risk: 
A nationwide registry study (AFNOR)

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Background: Stroke risk according to the CHA2DS2-VASc score guides oral anticoagulant (OAC) treatment in atrial fibrillation (AF) patients, and OAC is strongly recommended in patients with high stroke risk. There is less evidence of the clinical benefit of OAC in intermediate risk patients (non-sex CHA2DS2-VASc score of 1), and according to guidelines, OAC should be considered. However, the stroke risk is dynamic and an increase in the CHA2DS2-VASc score with a consequent change in the thromboembolic risk profile favoring OAC treatment is expected over time.

Purpose: To investigate the temporal changes in CHA2DS2-VASc score and the incidence of acquiring each of the CHA2DS2-VASc risk factors in AF patients at intermediate risk of stroke.

Methods: We identified 27,111 individuals with non-valvular AF aged ≥18 years, with a baseline CHA2DS2-VASc score of 1 (males) or 2 (females), in data from Norwegian national registries from 2011 through 2018. AF and stroke risk factors were identified with a minimum three-year look-back period. Individuals entered the study upon registration of a first-time AF diagnosis in combination with the first non-sex CHA2DS2-VASc risk factor, whichever came last. All participants were followed until an increase in the CHA2DS2-VASc score, death, emigration or study end. We calculated time from entry to an increased score (non-sex CHA2DS2-VASc score of ≥2) and assessed the cumulative proportions with an increase in CHA2DS2-VASc score per month. Average annual incidence rates for acquirement of new stroke risk factors were calculated as cases per 100 person-years (%/year) with 95% confidence intervals (CI).

Results: During a median follow-up time of 16 months (interquartile range: 4.9-36.6), 15,397 (56.8%) patients acquired at least one new stroke risk factor(s) (figure 1). One third of the patients who increased their CHA2DS2-VASc score, attained a new risk factor during the first four months of follow-up. The average annual risk of CHA2DS2-VASc score increment was 29% (95% CI: 28.6-29.5). The annual risk for a new risk factor was 23.2% for hypertension, 12.5% for age 65-74 years, 7.9% for heart failure, 6.2% for age ≥75 years, 5.4% for vascular disease, 2.4% for diabetes mellitus and 1.6% for thromboembolism (ischemic stroke, transitoric ischemic attack or systemic embolism) (figure 2).

Conclusion: AF patients at intermediate risk of stroke rapidly develop an increased stroke risk. In this nationwide study, more than half of AF patients at intermediate risk of stroke acquired a new risk factor during a median follow-up time of 16 months. The average annual risk of an increase in the CHA2DS2-VASc score was 29%. Intermediate-risk AF patients should be regularly reassessed, especially to avoid undertreatment if anticoagulation has previously been withheld.

Figure 1 Cumulative proportion (%) of AF patients at intermediate risk of stroke that attained a new risk factor during follow-up. During a median follow-up time om 16 months, 56.8% of all AF patients at Intermediate risk of stroke developed new risk factors and increased their CHA2DS2-VASc score to high risk (non-sex CHA2DS2-VASc score of ≥2). AF: Atrial Fibrillation
Figure 2 Annual risk of newly acquired risk factor components in AF patients at intermediate risk of stroke. The risk of an increase in the CHA₂DS₂-VASc score was 29% per year. Hypertension was the most frequently acquired risk factor, with an annual risk of 23% per year. AF: Atrial Fibrillation