

論文内容要旨

Impact of Previous Stroke on Clinical Outcome in Elderly Patients With Nonvalvular Atrial Fibrillation: ANAFIE Registry

(高齢非弁膜症性心房細動患者における脳卒中既往の臨床転
帰に対する影響：ANAFIE レジストリ)

Stroke, 2022, in press.

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The challenge in anticoagulant therapy in secondary prevention is the balance between the benefit of preventing ischemic events and the risk of bleeding, in particular intracranial hemorrhage. Both the risks of subsequent ischemic stroke (IS) and intracranial hemorrhage increase with increasing age. However, studies on the incidence of events and event risk factors in elderly patients with non-valvular atrial fibrillation (NVAF) and previous stroke/transient ischemic attack (TIA) are limited. The aim was to compare the long-term event incidence between elderly patients with NVAF and previous stroke/TIA and those without a history of stroke. Additionally, the effectiveness of direct oral anticoagulants (DOACs) was evaluated in patients with NVAF and previous stroke/TIA.

The ANAFIE Registry (UMIN Clinical Trials Registry UMIN000024006) is a prospective, multicenter, observational study of elderly Japanese patients (aged ≥ 75 years) with NVAF. All participants were registered from 1,273 medical institutions throughout Japan between October 2016 and January 2018 and followed up for 2 years. Data were collected at baseline and at 1 and 2 years. Patients were censored when primary and secondary endpoints occurred. Patients who met the following criteria were included in the Registry: 1) aged ≥ 75 years at enrollment, 2) definitive diagnosis of NVAF established by electrocardiographic findings, and 3) ability to attend specified clinic visits. Patients were divided into two groups according to history of stroke/TIA.

The primary endpoint of the present sub-analysis was the incidence of stroke/SE. The secondary endpoints were the incidence of the following events: major bleeding according to the International Society on Thrombosis and Hemostasis statement,¹⁵ IS, ICH, cardiovascular death, all-cause death, and net clinical outcome. Net clinical outcome was defined as a composite of stroke/SE, major bleeding, and all-cause death within 2 years. Cox models were used to determine whether there was a difference in the hazard of each endpoint in patients with/without history of stroke/TIA, and in IS/TIA survivors taking DOACs versus those taking warfarin.

Of the 33,062 patients enrolled, 787 were excluded due to protocol violation, withdrawal for site-related reasons, or loss to follow-up; the remaining 32,275 patients (13,793 women [42.7%]; median age, 81.0 years) were available for analysis. Of these, 7,303 patients (22.6%) had a history of stroke/TIA.

The mean follow-up period of patients with and without previous stroke/TIA was 1.86 and 1.89 years, respectively. Excluding those lost to follow-up, endpoints were assessed in 94.2% of patients in both groups. Compared with patients without previous stroke/TIA, patients with stroke/TIA had higher HRs of stroke/SE (primary efficacy outcome; 3.01/100 PY vs. 1.23/100 patient-years [PY]; adjusted HR 2.25, 95% CI 1.97–2.58), major bleeding, IS, ICH, and all-cause death. Thus, net clinical outcomes were higher in patients with previous

stroke/TIA (7.84/100 PY vs. 4.85/100 PY; adjusted HR 1.35, 95% CI 1.25–1.45) compared with those without previous stroke/TIA.

Of the 6,446 patients with previous IS/TIA, 4,393 (68.2%) were taking DOACs, and 1,668 (25.9%) were taking warfarin at enrollment. The risk of major bleeding (adjusted HR 0.67, 95% CI 0.48–0.94), ICH (HR 0.57, 95% CI 0.39–0.85), cardiovascular death (HR 0.71, 95% CI 0.51–0.99), and net clinical outcomes (HR 0.85, 95% CI 0.74–0.99) were lower in the DOAC group than in the warfarin group. However, risk of stroke/SE, IS, and all-cause death was comparable between both groups. No significant interactions were observed between each patient characteristic and medication for stroke/SE.

In conclusion, elderly Japanese patients with NVAF and previous stroke/TIA had higher HRs of stroke/SE, major bleeding, and all-cause death than those without previous stroke/TIA. Among patients with previous IS/TIA, the risk of hemorrhagic events was lower among patients treated with DOACs compared with warfarin.