



# Atrial fibrillation newly diagnosed after a stroke: which came first, atrial fibrillation or stroke?

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Atrial fibrillation (AF) is known to be a cause of ischemic stroke (1). However, paroxysmal AF (PAF) is often undetected because it is episodic, frequently asymptomatic, and has a short duration. In a meta-analysis, sequential stratified ECG monitoring detected AF in 11.5% of stroke survivors (95% confidence interval, 8.9–14.3%) (2). According to a report from the Framingham Study, most patients with AF diagnosed after stroke (AFDAS) eventually develop PAF or persistent AF (PerAF) (3). In other words, most cases of AFDAS are likely to be a cause rather than a consequence of stroke. Thus, anticoagulation therapy has been widely used for secondary prevention of stroke in these patients.

Recently, Sposato *et al.* proposed a new concept for AFDAS (4). They explained the concepts of predominantly cardiogenic AF and primarily neurogenic AF. Preexisting AF is most likely to be caused by prestroke cardiac structural changes; thus, the arrhythmia could be considered as predominantly cardiogenic AF. On the contrary, newly diagnosed AF may be the consequence of stroke and therefore can be regarded as primarily neurogenic AF. Despite this new classification, the characteristics of AFDAS remain unclear.

In a recent report in *Neurology* (5), Sposato *et al.* investigated the characteristics and stroke recurrence rates of AFDAS compared with AF known before stroke (KAF). They used a large observational dataset from the Ontario Stroke Registry, which included >23,000 patients, and compared the risk of recurrent stroke and prevalence of heart disease in three different groups of patients with

acute ischemic stroke: those with sinus rhythm (SR), those with AFDAS (newly diagnosed AF during hospital stay for ischemic stroke), and those with KAF. In their cohort of 23,376 patients, 587 had AFDAS and 6,904 had KAF. The rate of occurrence of ischemic stroke after 1 year was similar in patients with SR (8.0%) and AFDAS (7.0%) but higher in those with KAF (9.6%,  $P<0.001$ ). Patients with AFDAS and those with SR had no difference in the adjusted risk of recurrent stroke (hazard ratio, 0.90; 95% confidence interval, 0.63–1.30;  $P=0.57$ ). Patients with KAF had a higher prevalence of heart disease than those with AFDAS (coronary artery disease, 34.7% *vs.* 18.2%,  $P<0.001$ ; myocardial infarction; 20.5% *vs.* 11.6%,  $P<0.001$ ; heart failure; 16.8% *vs.* 5.5%,  $P<0.001$ ). The results of the study suggested that the underlying pathophysiology of AFDAS may differ from that of KAF. If a neurogenic mechanism of AFDAS is present, patients with neurogenic AFDAS may have a lower recurrence rate of AF and consequently have a lower rate of stroke and heart disease. Thus, the concept of neurogenic AF may shed new light to the relationship between AF and stroke.

As the authors described, there were several limitations in this study. Because the study was an observational study, cardiac monitoring and AF detection workup were not standardized. The rate of AFDAS (only 2.5% of patients) was lower than that in a previous study (2); therefore, underdiagnosis of PAF is of concern. Moreover, the study lacked information regarding the mechanism of incident or recurrent ischemic stroke, proportion of patients with PAF *vs.* PerAF in each group, and topography of brain infarcts.

These factors may have influenced the outcomes.

Although there are several limitations in the study, it is no wonder that patients after stroke would develop arrhythmia caused by neurogenic mechanism. In fact, it is well known that a number of cardiac changes occur after the acute phase of subarachnoid hemorrhage, including ECG changes, structural changes on echocardiography, and acute troponin level elevation (6). Moreover, a prospective study of 501 patients with ischemic stroke showed that serious arrhythmia was detected in 126 patients in the first 72 h after admission due to acute stroke (including 57 patients with AF), and the incidence of arrhythmia was the highest in the first 24 h after admission (7). The potential mechanism of these arrhythmias is autonomic imbalance (vagal dominance replaced by increased sympathetic tone) (8).

Thus, what occurs first, atrial fibrillation or stroke? We should be careful to distinguish AFDAS from preexisting but newly diagnosed AF. Further study is required to elucidate the concept, definition, subtypes, AF recurrence rate, and secondary prevention strategy of AFDAS.

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