Acute interatrial block is a distinct risk factor for ischemic stroke

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The last few decades have given rise to extensive research focused on atrial conduction disorders, identified by ECG, and their clinical relevance. Most notably, the observed associations of interatrial block, supraventricular arrhythmias, and increased risk of cardiovascular mortality have driven further research, and in particular into determining the role of interatrial block as a novel risk factor of stroke. Interatrial blocks are characterized by P-wave duration ≥120 ms with left atrial retrograde activation that signifies a conduction delay between the left and right atria.[1] Similar to other types of heart block, interatrial block may be partial (first-degree) or advanced (third-degree).[1] Advanced interatrial block (aIAB), also termed Bayés syndrome, indicates atrial fibrosis and abnormal cardiac modeling. Although common in patients with aIAB,[1,2] left atrial enlargement is not a necessary component of a diagnostic criteria.

One percent of the global population and 2% of patients with valvular heart disease and cardiomyopathies have aIAB.[3] The prevalence of aIAB increases with age and in those in the general population with stroke risk factors: coronary artery disease, hypertension, hypercholesterolemia, smoking, obesity, sedentary lifestyle, and atrial fibrillation (AF).[4,5] aIAB is also associated with increased all-cause cardiovascular disease and stroke mortality.[4,5] Further, Bayés de Luna demonstrated that aAIB is a strong risk factor for incident atrial flutter and fibrillation.[6] This positions aIAB as a well-described but poorly recognized cardiac rhythm disorder with important clinical implications.[1]

In this issue of *Neurology*®, O'Neal et al.[7] present findings from the Atherosclerosis Risk in Communities Study of 14,716 adults with digital ECG measured at baseline and within the first 10 years, then followed for more than 20 years for incident ischemic stroke events. Among those with evidence of aIAB (1.8%), the incidence rate of ischemic stroke was more than twice that of those without aIAB. Further, aIAB was associated with more than a 1.5-fold increased risk of incident ischemic stroke after adjustment for traditional stroke risk factors. The observed relationship between aAIB and ischemic stroke in this large cohort did not differ by race, age group (<54 and ≥54 years at baseline), or sex.

Perhaps the most important finding, the independence of aIAB from AF (hazard ratio [HR] and 95% confidence interval [95% CI] 1.70 [1.18–2.44]) and P-wave terminal force in lead V_1 (HR [95% CI] 1.54 [1.07–2.22]), underscore the potential of aIAB as a novel risk factor for ischemic stroke. Both aIAB and P-wave terminal force, interrelated forms of P-wave abnormalities, are known risk factors for AF. Yet the independence of aIAB from AF suggests that the stroke risk associated with aIAB is not mediated by nonparoxysmal forms of AF.

This work underscores the importance of an evolving literature that indicates aIAB and other atrial cardiopathies as emerging risk factors for clinical ischemic stroke events and cardiovascular mortality. Future studies will need to examine these relationships in more detail and in nuanced fashion. For example, partial intra-atrial blocks may also increase risk for clinical or subclinical stroke. This work by O'Neill et al.[7] examined the clinically defined stroke and periodic assessments of AF. Future studies may provide novel insights into relationships among inter-atrial block, paroxysmal AF, and subclinical cerebrovascular disease associated with ischemia and cardioembolic stroke, namely subclinical infarcts and white matter disease. Finally, future combinations of cardiac MRI with ECG studies may also illuminate the structural and hemodynamic functional consequences of aIAB and its role in cerebrovascular risk.

To treat or not to treat? The strong relationship between aIAB and AF has led researchers to investigate the prevention of atrial arrhythmias using antiarrhythmic drugs in patients with aIAB.[8] Initial placebo-controlled studies in aIAB show positive findings that prophylactic antiarrhythmic intervention reduces AF recurrences over long-term follow-up.[8] The data presented herein by O'Neill et al. provide Class III evidence that aIAB is a risk factor for ischemic stroke independent of AF. Among individuals with aIAB, anticoagulation strategies might also reduce morbidity and mortality

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from stroke—this warrants further investigation. The relatively low prevalence of aIAB in the general population is unlikely to lead to the development of broad screening efforts and direct clinical focus on identifying risk factors for aIAB. For this to happen, additional epidemiology studies will need to define further the exact risk profiles for aIAB.

Along with deep negativity of the P-wave in V_1 and AF, aIAB is among the most important atrial ECG predictors of cardiovascular death and ischemic stroke. Future observational studies will need to elucidate the determinants and risk factor profiles for aIAB, the extent of ischemic stroke risk within P-wave abnormalities, and the efficacy of treating aIAB to prevent both AF and ischemic stroke. These data support an emerging conceptualization of a role of the cardiac left atrium in stroke risk and stroke prevention and suggest a broader relevance of atrial dysfunction for stroke risk.

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