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Research Letter

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Ischemic stroke severity and mortality after left atrial appendage closure vs nonwarfarin oral anticoagulants in patients with prior stroke

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In a multicenter observational study of stroke severity after various stroke prevention strategies, we recently demonstrated that ischemic stroke (IS) in patients with atrial fibrillation (AF) who had received left atrial appendage closure (LAAC) is less often disabling/fatal than IS in patients receiving non–vitamin K oral antagonists (NOACs).[1] However, patients with AF and prior IS are distinguished by a higher propensity for recurrent stroke and greater resulting neurological disability and mortality.[2] Accordingly, it is crucial to optimize secondary stroke prevention. In this subanalysis, we compared IS severity in patients with AF and prior stroke receiving LAAC vs NOAC.

We performed a retrospective analysis of consecutive patients with nonvalvular AF at 8 centers who had a history of stroke and then presented with recurrent (index) IS after either LAAC implantation (Watchman [Boston Scientific Inc, Marlborough, MA], WATCHMAN FLX [Boston Scientific Inc, Marlborough, MA], Amplatzer Cardiac Plug [Abbott Inc, Lake County, IL], or Amulet [Abbott Inc, Lake County, IL] [IS_{LAAC} group]) or anticoagulation with a NOAC (apixaban, rivaroxaban, dabigatran, or edoxaban [IS_{NOAC} group]) for at least 7 days before hospital admission. Patients with valvular AF, rheumatic heart disease, hemorrhagic stroke, undetermined stroke type, periprocedural stroke (within 7 days of a procedure), IS occurring during hospitalization for another condition, transient ischemic attack, or recurrent IS within 90 days of index IS were excluded. The primary outcome was disabling/fatal stroke (modified Rankin Scale [mRS] score 3–6) at discharge and at 3 months. The secondary outcome was all-cause mortality at 3 months.

Of 447 patients, 202 (45.2%) had prior IS, transient ischemic attack, or hemorrhagic stroke: 141 and 61 in the IS_{NOAC} and IS_{LAAC} groups, respectively. Compared with the IS_{NOAC} group, the IS_{LAAC} group more often had a history of bleeding (59.0% vs 29.8%; $P < .001$) and hemorrhagic stroke (29.5% vs 8.5%; $P < .001$) but less carotid artery disease (19.7% vs 40.4%; $P = .006$). Mean age (74.3 ± 14.3 years vs 72.5 ± 12.0 years; $P = .35$), CHA_2DS_2-VASc scores (5.4 ± 1.1 vs 5.6 ± 1.5; $P = .46$), and HAS-BLED scores (3.7 ± 1.1 vs 3.4 ± 1.2; $P = .10$) were comparable between groups.

Although the median (interquartile range) admission mRS scores were similar (3.0 [2–4] vs 3.0 [2–4]; $P = .42$), mRS scores at discharge (2.0 [1–3] vs 4.0 [2–4]; $P < .001$) and at 3 months (1.5 [0.75–3.0] vs 3.0 [1–6]; $P = .002$) were significantly lower in the IS_{LAAC} group than in the IS_{NOAC} group. The primary and secondary outcomes are depicted in Figure 1. The rate of hemorrhagic transformation (HT) identified by brain imaging was numerically higher in the IS_{NOAC} group than in the IS_{LAAC} group (21.3% vs 11.5%; $P = .11$); this difference did not reach statistical significance. Furthermore, patients in the IS_{LAAC} group were more likely to receive thrombolytics than those in the IS_{NOAC} group (27.9% vs 9.9%; $P = .002$) while there was no significant difference in the rate of endovascular

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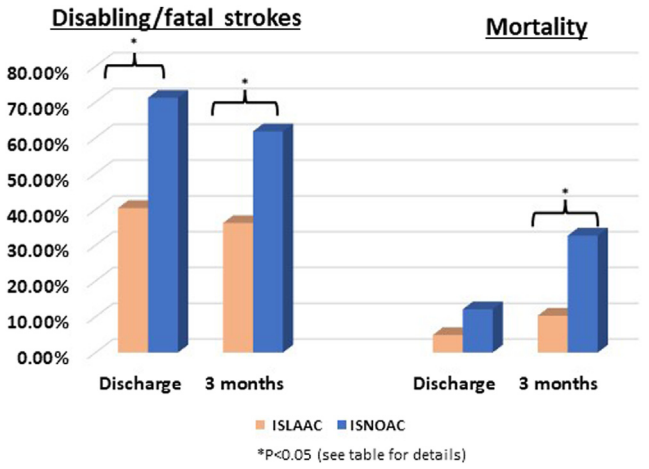

Figure 1
Disabling/fatal stroke and mortality in the ischemic stroke after left atrial appendage closure and ischemic stroke after non-vitamin K oral antagonists groups.

thrombectomy between the 2 groups (18% vs 12.1%; $P = .27$). Multivariate regression analysis including variables such as CHA_2DS_2-VASc score, HAS-BLED score, smoking, prior major bleeding, paroxysmal AF, carotid disease, medication adherence, HT, thrombolysis, and IS_{LAAC} found IS_{LAAC} independently associated with fewer disabling/fatal strokes at discharge (odds ratio [OR] 0.20; 95% confidence interval [CI] 0.08–0.45; $P < .001$) and at 3 months (OR 0.25; 95% CI 0.09–0.71; $P = .01$) and fewer deaths at 3 months (OR 0.16; 95% CI 0.04–0.63; $P = .008$).

This analysis demonstrates that in patients with AF and prior stroke, recurrent IS less often disabling or fatal with a secondary stroke prophylaxis strategy of LAAC than with NOAC. The mechanism underlying the reduced stroke severity in the IS_{LAAC} group is unclear. One potential explanation involves a decrease in thromboembolic burden by LAAC compared with NOAC treatment. Another possibility is more frequent or severe HT after IS in NOAC-treated patients than in those who received LAAC. This study focused on functional outcomes using the mRS and lacked the requisite vascular and brain imaging data to validate this hypothesis. The underlying mechanisms contributing to increased mortality after recurrent stroke are also unclear, but it is likely that greater neurological deficit renders individuals more susceptible to complications resulting in poor prognosis.[3] Limitations of this analysis include its nonrandomized retrospective design with residual confounding factors potentially influencing the choice of stroke prevention strategies, and the absence of baseline mRS assessments, though there was no significant difference in admission mRS scores between the 2 groups, and changes in mRS scores from before to after stroke has limited validity. The findings provide a foundation for randomized trials comparing the outcomes of LAAC and NOAC therapies in patients with AF and prior stroke.

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