

Ischemic Stroke Mandates Cross-Disciplinary Collaboration

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The fields of cardiology and stroke medicine encompass the 2 most important vascular territories impacted by disease, those involving the heart and brain. The 2 disciplines share many important commonalities, and the most important overlap between cardiology and stroke medicine involves ischemic heart disease and ischemic stroke. Commonalities between these 2 frequently encountered disorders include involvement of physicians and researchers with a wide range of training backgrounds and skill sets, similar epidemiological bases and risk factors, overlapping pathophysiological mechanisms, and similar approaches to acute therapy and to primary and secondary prevention. In addition, ischemic stroke from a cardiac or aortic source has been increasingly identified.¹ Clinicians and researchers from each discipline need to be aware of advances in both fields to optimize patient care and research. *Circulation* and *Stroke*, leading journals in their respective fields, endeavor to promote this effort and to foster cooperation between clinicians and researchers from both disciplines.

Two commonly encountered cardiovascular disorders that illustrate the overlap between cardiology and stroke medicine are patent foramen ovale (PFO)-related stroke and primary/secondary stroke prevention in patients with atrial fibrillation. PFOs exist in ≈20% to 25% of the population, occurring more frequently in women than men.² In a stroke patient with a PFO in whom all other potential causes have been excluded, the PFO becomes the presumed culprit of the infarct. Both cardiologists and stroke physicians frequently encounter such patients, and until recently the best approach for secondary stroke prevention was uncertain. Recent publication of 2 clinical trials, the GORE REDUCE trial³ (Gore Cardioform Septal Occluder for Patent Foramen Ovale [PFO] Closure in Stroke Patients) and the CLOSE trial (Patent Foramen Ovale Closure or Anticoagulant Versus Antiplatelet Therapy to Prevent Stroke Recurrence),⁴ coupled with the publication of the long-term outcome results of the RESPECT trial (Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment)⁵ has helped to clarify treatment decisions.

The results of these 3 trials provide clear evidence that PFO closure is more effective than medical therapy for

secondary stroke prevention in patients under the age of 60 with a high-risk PFO, that is, one associated with substantial degree of shunting from the right to left atrium and an atrial septal aneurysm. All 3 trials excluded non-PFO-related stroke causes, such as large- and small-vessel disease, another cardiac stroke source, and a hypercoagulable disorder. With these new findings in hand, evaluation and management of ischemic stroke patients with a PFO require collaboration between cardiologists and stroke physicians more than ever. In approving the Amplatzer device for PFO closure in patients with PFO-related stroke, the US Food and Drug Administration recognized the need for evaluation by both a cardiologist and a neurologist (stroke physician) to confirm the accuracy of the diagnosis and to exclude other potential causes of ischemic stroke.⁶ In fact, we speculate that payers will mandate evaluation by both cardiologists and neurologists (stroke physicians) before reimbursement for a closure procedure is approved.

We advocate that cardiologists and stroke physicians establish institutional guidelines for the evaluation and treatment of potential PFO-related stroke patients and strongly consider developing jointly staffed clinics to expedite the evaluation of such patients. In addition to PFO-related strokes, such a joint clinic could also evaluate other types of stroke patients that have a cardiac or vascular source, such as those with embolic stroke of undetermined cause, aortic arch-related stroke, cardiomyopathy-related stroke, stroke related to cardiac valve disorders and other uncommon cardiac stroke sources, such as atrial myxoma and fibroelastoma. Each of these disorders will benefit from cross-disciplinary collaborations that bridge diverse areas of expertise.

Atrial fibrillation is an increasingly recognized cardiac arrhythmia that is the presumed cause for ≈25% of ischemic strokes in Western countries.⁷ Ischemic stroke is 1 of the 2 most important complications of atrial fibrillation, along with chronic heart failure.^{1,8} Cardiologists are most commonly involved with initiating primary stroke prevention treatment, whereas stroke physicians typically see patients after a presumed atrial fibrillation-related stroke has occurred and remain involved with treatment decisions for secondary prevention. For ischemic stroke patients with a single or multiple end-vessel territory infarct without an obvious explanation for their stroke after initial evaluation with brain and vessel imaging, a comprehensive search for atrial fibrillation is usually initiated. This evaluation begins with inpatient ECG monitoring via telemetry or a 24-hour Holter monitor and continues with prolonged, continuous outpatient ECG monitoring, typically for up to 30 days with a variety of outpatient monitoring devices.⁹ In some patients, an implantable monitor can be used that allows for months of continuous monitoring. The detection of intermittent, paroxysmal atrial fibrillation after an unexplained ischemic stroke is time dependent; the longer the patient is monitored the

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more likely atrial fibrillation will be detected.¹⁰ Stroke physicians ordering the monitoring are dependent on their cardiology colleagues and their hospitals to make the monitoring device available and to interpret the results.

If paroxysmal atrial fibrillation is detected, either the cardiologist or the stroke physician can initiate a secondary prevention regimen, with either warfarin or with 1 of the 4 newer direct-acting oral anticoagulants. Each of the direct-acting oral anticoagulants has relative advantages and disadvantages, so a discussion between the cardiologist and stroke physician of individual patient factors will be useful for determining which one is the best for a particular patient. For example, in a patient with an atrial fibrillation–related stroke in whom a recurrent ischemic stroke is the most important consideration because the patient has had several prior atrial fibrillation–related strokes or acute infarcts in multiple vascular territories, dabigatran would seem to be the best choice because it was the only one of the direct-acting oral anticoagulants in its clinical trial to significantly reduce ischemic stroke occurrence in patients with good renal function when compared with warfarin.¹¹ In a patient with atrial fibrillation–related stroke in whom the risk of major bleeding is a concern, apixaban would be the preferred choice because the risk of major bleeding was significantly lower than with warfarin.¹² Manifestly, cardiologists and stroke physicians are dependent on each other for the optimal evaluation of patients with unexplained stroke in whom atrial fibrillation is a possible cause and should also collaborate in the determination of the best approach for secondary stroke prevention. A jointly staffed clinic may be the ideal setting for such interaction.

Circulation and *Stroke* encourage our readers to work closely together to improve the identification and treatment of ischemic stroke caused by a cardiac or aortic disorder. A few common examples of ischemic stroke related to an underlying cardiac disorder are listed here, but several others also lend themselves to joint evaluation by cardiologists and stroke physicians, expanding opportunities for productive collaboration between the 2 disciplines yet further. The expertise provided by cardiologists and stroke physicians in jointly evaluating and managing stroke related to a cardiac or aortic source is indeed synergistic and complementary. By working together, we can provide optimal care for our patients to efficiently and in a cost-effective manner better

identify and help reduce the increasing burden of ischemic stroke from cardiac sources.

Disclosures

None.

References

1. Fisher M, McAllister M. Cardiological aspects of stroke prevention. *Circ J*. 2015;79:271–277. doi: 10.1253/circj.CJ-14-1342.
2. Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. *Mayo Clin Proc*. 1984;59:17–20.
3. Søndergaard L, Kasner SE, Rhodes JF, Andersen G, Iversen HK, Nielsen-Kudsk JE, et al; Gore REDUCE Clinical Study Investigators. Patent foramen ovale closure or antiplatelet therapy for cryptogenic stroke. *N Engl J Med*. 2017;377:1033–1042. doi: 10.1056/NEJMoa1707404.
4. Mas JL, Derumeaux G, Guillon B, Massardier E, Hosseini H, Mechtouff L, et al; CLOSE Investigators. Patent foramen ovale or anticoagulation vs. antiplatelets after stroke. *N Engl J Med*. 2017;377:1011–1021. doi: 10.1056/NEJMoa1705915.
5. Saver JL, Carroll JD, Thaler DE, Smalling RW, MacDonald LA, Marks DS, et al; RESPECT Investigators. Long-term outcomes of patent foramen ovale closure or medical therapy after stroke. *N Engl J Med*. 2017;377:1022–1032. doi: 10.1056/NEJMoa1610057.
6. Farb A, Ibrahim NG, Zuckerman BD. Patent foramen ovale after cryptogenic stroke - assessing the evidence for closure. *N Engl J Med*. 2017;377:1006–1009. doi: 10.1056/NEJMp1700218.
7. Pistoia F, Sacco S, Tiseo C, Degan D, Ornello R, Carolei A. The epidemiology of atrial fibrillation and stroke. *Cardiol Clin*. 2016;34:255–268. doi: 10.1016/j.ccl.2015.12.002.
8. Kotecha D, Chudasama R, Lane DA, Kirchhof P, Lip GY. Atrial fibrillation and heart failure due to reduced versus preserved ejection fraction: a systematic review and meta-analysis of death and adverse outcomes. *Int J Cardiol*. 2016;203:660–666. doi: 10.1016/j.ijcard.2015.10.220.
9. Thijs V. Atrial fibrillation detection: fishing for an irregular heartbeat before and after stroke. *Stroke*. 2017;48:2671–2677. doi: 10.1161/STROKEAHA.117.017083.
10. Sanna T, Diener HC, Passman RS, Di Lazzaro V, Bernstein RA, Morillo CA, et al; CRYSTAL AF Investigators. Cryptogenic stroke and underlying atrial fibrillation. *N Engl J Med*. 2014;370:2478–2486. doi: 10.1056/NEJMoa1313600.
11. Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, Parekh A, et al; RE-LY Steering Committee and Investigators. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2009;361:1139–1151. doi: 10.1056/NEJMoa0905561.
12. Granger CB, Alexander JH, McMurray JJ, Lopes RD, Hylek EM, Hanna M, et al; ARISTOTLE Committees and Investigators. Apixaban versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2011;365:981–992. doi: 10.1056/NEJMoa1107039.

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