Voice of Stroke — April 2026

Episode 3: Atrial Fibrillation and Stroke Prevention – What's New?

Introduction: Welcome to Voice of Stroke – your rapid, reliable update on the science advancing stroke care – brought to you by the European Stroke Organisation.

Body: Atrial fibrillation is responsible for up to a quarter of all ischaemic strokes. Even when patients are on appropriate anticoagulation, there remains a non-negligible residual risk of stroke and other cardiovascular events. So while our current treatments are effective, there is clearly still room for improvement.

In this episode of Voice of Stroke, we are going to look at four important recent studies.

- First, two *New England Journal of Medicine* trials asking whether left atrial appendage closure could replace oral anticoagulation in patients who are otherwise eligible for it.
- Second, a *JAMA Neurology* study evaluating whether adding catheter ablation to standard care reduces the risk of recurrent stroke.
- And finally, a large population-based study in *Heart Rhythm*, looking at blood pressure control and why it may matter more than we think, particularly for young patients with AF.

Let's start. When we think about stroke prevention in atrial fibrillation, anticoagulation remains the cornerstone and this is backed by very strong evidence. Direct oral anticoagulants have transformed our ability to protect patients.

However, anticoagulation has its limitations. There is bleeding risk, adherence challenges, and potential drug interactions. Not every patient tolerates long-term therapy well. This has led to growing interest in alternative approaches, such as closing off the left atrial appendage. This is the part of the heart where about 90% of AF-related clots form. Whilst device based closure can potentially reduce long-term bleeding risk, it comes with its own periprocedural risks. Currently, this approach is mainly used in patients who can't take anticoagulation, such as those with very high bleeding risk. So the next question is: what about those who

can?

Two trials published recently in the New England of Journal of Medicine addressed this question and came to slightly different conclusions.

Let's start with the CLOSURE-AF trial. This was an investigator-led, multicenter, non-inferiority trial from Germany, enrolling patients who are at high risk of both stroke and bleeding. The investigators compared device-based percutaneous left atrial appendage closure with best medical care.

Over 900 patients were included. The mean age was 78 years. The mean CHA2DS2-VASc score was 5 and the mean HAS-BLED score was 3. A third of the patients had history of TIA or ischaemic stroke. About 85% of the patients in the medical-therapy group received a DOAC. There was no restriction in the choice of the closure device, as long as the device had been CE mark approved.

What did they find? The trial did not show that device closure was non-inferior to medical therapy. In fact, after a median follow-up of 3 years, the composite outcome, including stroke, systemic embolism, major bleeding, or death was more common in the device group. There were also more serious complications, including major bleeding requiring transfusion and pericardial tamponade in the device group.

Now let's compare that to the larger CHAMPION-A-F trial.

This was an industry sponsored, international trial that enrolled 3000 patients who were eligible for anticoagulation. The patients were generally younger with lower stroke and bleeding risks than those in CLOSURE-AF. They were randomised to left atrial appendage closure using the WATCHMAN device or oral anticoagulation with a NOAC. The primary efficacy endpoint was a composite of cardiovascular death, stroke, or systemic embolism, tested for non-inferiority. The primary safety endpoint was non-procedure-related major bleeding, tested for superiority.

Here are the results.

After three years, the primary outcome happened in about 6% of people with the device, compared to just under 5% in those taking a NOAC. So, a slightly higher risk with the device—about a 1% difference. Importantly, the study met its criteria for non-inferiority. In simple terms, the device performed broadly similarly to anticoagulation, even if it didn't outperform it.

Where things start to differ is safety. Major bleeding unrelated to the procedure happened in about 11% of people with the device, compared to 19% of those on anticoagulants. So that's a meaningful reduction in bleeding. However, when procedure-related bleeding events were included, the bleeding advantage for the device group diminished substantially. From a stroke perspective, ischaemic stroke or systemic embolism occurred in about 3% of the patients in the device group and in 2% of those in the anticoagulation group and there was no differences in the incidence of haemorrhagic stroke, which we are mostly worried about.

So two trials, similar patient populations, but apparently different results.

Overall, left appendage closure remains a reasonable option for patients who cannot tolerate anticoagulation. But for those who can, we still don't have enough evidence to confidently replace anticoagulation with closure. Ongoing trials, such as CATALYST and OCCLUSION-AF will hopefully shed more light in this population. There are also trials looking at left appendage closure in addition to anticoagulation in patients with AF and breakthrough strokes, which are also of particular interest to stroke physicians.

Let's now move on to our second part. One of the most exciting developments in AF management over recent years has been the concept of rhythm control to reduce vascular events. The EAST-AFNET 4 trial showed that early rhythm control reduces the risk of stroke and heart failure in patients with AF.
This naturally raises the follow-up question: could catheter ablation, the most effective rhythm control strategy we have, reduce the risk of recurrent stroke? That's what the STABLED trial set out to answer.

STABLED was a relatively small Japanese trial, enrolling 251 patients who had an AF-related stroke and were on edoxaban. Patients were randomized to either catheter ablation plus standard therapy, or standard therapy alone. The primary outcome was a composite of recurrent ischaemic stroke, systemic embolism, all-cause death, and hospitalisation for heart failure.

Did ablation work? In short, no.

The trial was neutral. The composite primary endpoint occurred in approximately 5% of patients in both groups, with no statistically significant difference between arms. On the positive side, procedural complications were very low, under 1%.

So for now, we don't have evidence that catheter ablation reduces recurrent stroke risk in this population. For the broader question, whether rhythm control improves secondary stroke prevention, remains open. The ongoing EAST-STROKE trial should give us more answers in the near future.

Our last study shifts to population-level epidemiology, but may have the most immediate clinical relevance.

This was a large nationwide study from South Korea, including over 300,000 patients with newly diagnosed AF. Patients were followed for a median of six years and the investigators looked at how blood pressure related to stroke and mortality.

The headline finding is striking. Elevated blood pressure has a much stronger impact on stroke risk in younger AF patients. For example, in patients in their 40s, having a systolic blood pressure of 160 or higher was associated with more than a threefold increase in stroke risk. But in patients aged 70 and above, that increase was much smaller. So the relative impact of hypertension clearly declines with age.

What about all-cause mortality? Instead of a straight line, it's U-shaped. Patients with very low systolic blood pressure, below 100, actually had the highest mortality. And those in the 100 to 120 range did better.

So what does this mean for practice? First, blood pressure management should perhaps also be a key priority in AF patients alongside anticoagulation. Second, young patients with AF may benefit the most from aggressive BP control.

So to wrap up:

- Left atrial appendage closure is a reasonable alternative for patients who cannot take anticoagulation due to contraindications or intolerance, but more data are needed before using it in those who can
- In patients with AF-related stroke, catheter ablation did not reduce recurrent vascular events compared to standard care alone, but larger trials are ongoing looking at the role of rhythm control more generally in secondary prevention
- And finally, blood pressure control may be just as important as anticoagulation in patients with AF, especially at younger ages

Full references and links to all the studies discussed are available in the episode notes.

Ending: That's all for this episode of Voice of Stroke, brought to you by the European Stroke Organisation. You can listen to Voice of Stroke on all your favourite podcast channels, including Spotify and Apple. Visit the European Stroke Organisation E-S-O-dash-stroke-dot-org for more information about our organisation, mission and our key activities. I'm Linxin Li. Thanks for listening.

Credit: This episode was written by Voice of Stroke Podcast editor Umberto Pensato and editor-in-chief Linxin Li.

References

1. Landmesser U et al. Left Atrial Appendage Closure or Medical Therapy in Atrial Fibrillation. N Endl J Med. 2026; 394: 1270-1280. doi: 10.1056/NEJMoa2513310. https://www.nejm.org/doi/full/10.1056/NEJMoa2513310

2. Doshi SK et al. Left Atrial Appendage Closure or Anticoagulation for Atrial Fibrillation. N Engl J Med. 2026 Mar 28. doi: 10.1056/NEJMoa2517213 https://www.nejm.org/doi/full/10.1056/NEJMoa2517213

3. Kimura K et al. Catheter Ablation and Oral Anticoagulation for Secondary Stroke Prevention in Atrial Fibrillation: The STABLED Randomized Clinical Trial. JAMA Neurol. 2026 Mar 2:e260155. doi: 10.1001/jamaneurol.2026.0155. https://jamanetwork.com/journals/jamaneurology/fullarticle/2845745

4. Jeong MH et al. Impact of blood pressure on the risk of stroke and all-cause mortality in patients with atrial fibrillation across different age groups: a nationwide population-based study. Heart Rhythm. 2026 Mar 24:S1547-5271(26)02172-7. doi: 10.1016/j.hrthm.2026.03.1917. https://www.heartrhythmjournal.com/article/S1547-5271(26)02172-7/fulltext