Voice of Stroke — June 2026

Episode 5: Blood Pressure Control: Which Patients May Benefit Most From Specific Strategies?

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

In this episode of Voice of Stroke, we focus on one of the most important and practical challenges in vascular prevention: How should we think about hypertension in 2026? The question now is no longer simply whether to lower blood pressure. Instead, we are asking which treatments work best, who to treat, and how hypertension-related vascular disease may influence stroke mechanisms and secondary prevention.

Today, we will discuss three recent studies that may help answer these questions.

- First, we will review two large meta-analyses published in *the Lancet and JAMA* examining the efficacy and tolerability of antihypertensive drugs and their combinations.
- Second, we will discuss an individual patient data meta-analysis published in *the European Heart Journal*, investigating blood pressure lowering in isolated diastolic hypertension.
- Finally, we will discuss an exploratory analysis of the ARCADIA trial, published in *JAMA Neurology*, which explored whether markers of high-risk hypertension modify the response to anticoagulation after cryptogenic stroke.

Let's start with two related studies that help to answer a practical question we face every day in clinic: which antihypertensive drugs work best, and which are best tolerated?

The first study, published in The Lancet was a systematic review and meta-analysis of nearly 500 randomised, double-blind, placebo-controlled trials evaluating the blood pressure-lowering efficacy of the major antihypertensive drug classes and their combinations. The mean age of the patients was 54 years with a mean follow up of 9 weeks.

The key finding was that not all antihypertensive regimens are equally potent. Blood pressure reduction varied substantially according to drug class, dose, baseline blood pressure, and whether drugs were used in combination. As expected, combination therapy produced substantially greater blood pressure reductions than monotherapy, and the investigators used these data to develop an online tool that can predict the expected blood pressure reduction from different treatment regimens.

The second study, published in JAMA in May 2026, addressed the other side of the equation: tolerability. In this network meta-analysis of more than 700 short-term trials, the investigators compared adverse effects and treatment discontinuation across antihypertensive drug classes and combinations.

Perhaps surprisingly, several combination therapies were better tolerated than monotherapy and even placebo. The best-tolerated regimen was a combination of an angiotensin receptor blocker, or ARB, together with a calcium channel blocker. Four of the five highest-ranked regimens contained an ARB. In contrast, some beta-blocker diuretic combinations were associated with higher rates of treatment discontinuation due to adverse effects.

Taken together, these studies challenge the traditional stepwise approach of starting with monotherapy and only adding additional agents later. Combination therapy is not only more effective at lowering blood pressure, but certain combinations may also be as well tolerated or even better tolerated than monotherapy. These findings provide further support for the growing emphasis on early combination therapy in contemporary hypertension guidelines.

So far we discussed how to treat hypertension. The next study, published in the European Heart Journal, looked at who we should treat, particularly whether we should treat isolated diastolic hypertension, a topic that has been debated for decades.

In this individual patient data meta-analysis from the Blood Pressure Lowering Treatment Trialists' Collaboration, more than 350,000 participants from 51 randomised trials were included. Isolated diastolic hypertension was defined as systolic blood pressure below 130 mmHg and diastolic blood pressure of at least 80 mmHg.

Overall, nearly 16,000 participants were identified as having isolated diastolic hypertension at baseline, representing about 4% of the study population. As expected, these patients tended to be younger and were less likely to be women.

During a median follow-up of approximately 4 years, more than 43,000 major cardiovascular events occurred. The key finding was reassuring: the cardiovascular benefits of blood pressure lowering were similar regardless of whether patients had isolated diastolic hypertension or not. For every 5 mmHg reduction in systolic blood pressure, the risk of major cardiovascular events was reduced by approximately 9% in patients with isolated diastolic hypertension and by 10% in those without. Similar findings were observed for all-cause mortality and the individual components of the primary outcome including for stroke. Results were also consistent across age groups and in patients with and without prior cardiovascular disease.

The study also addressed the long-discussed diastolic "J-curve" concern. Across baseline diastolic blood pressure values ranging from 60 to 90 mmHg, there was no clear evidence that treatment benefit diminished at lower diastolic pressures. These findings are consistent with post hoc analyses from trials such as SPRINT and with Mendelian randomization studies, which also did not support a causal J-curve relationship.

What are the clinical implications? This analysis provides the strongest randomised evidence to date that isolated diastolic hypertension should not be considered a special category in which blood pressure lowering is less effective. This is particularly important because treatment rates remain low among patients with isolated diastolic hypertension, especially in younger adults. Whilst primary prevention guidelines recommend a comprehensive risk assessment for treatment decisions, from a stroke perspective, clinicians should not hesitate about treating blood pressure particularly in young stroke patients with isolated diastolic hypertension.

That brings us to the last paper, an exploratory analysis of the ARCADIA trial, published in *JAMA Neurology* in April this year.

The ARCADIA trial was a multicenter, randomised trial comparing apixaban versus aspirin for the prevention of recurrent stroke in patients with a recent cryptogenic stroke and atrial cardiopathy without atrial fibrillation. The trial was stopped early for futility with identical annualised recurrent stroke rates of 4.4% in both groups.

One explanation for the neutral ARCADIA result is that current stroke classification systems may not fully capture hypertension-related cerebrovascular disease. If a substantial proportion of recurrent events in these patients are actually driven by hypertensive arteriopathy rather than occult cardioembolism, any benefit of anticoagulation could be diluted. To test this hypothesis, the investigators asked in this exploratory analysis:

was the effect of anticoagulation compared to antiplatelet therapy modified by the presence of hypertension with high-risk features in the ARCADIA trial population.

Before we dive into the results, how was hypertension with high-risk features defined?

The authors used a framework similar to that proposed in the 2023 European Society of Hypertension guidelines. The primary definition of hypertension with high-risk features was a baseline systolic blood pressure of at least 160 mm Hg or left ventricular hypertrophy on echocardiography. Several secondary definitions were also examined, including eGFR less than 60.

What did they find? Of the 1,015 patients enrolled in ARCADIA, 95% had both blood pressure and Echo data available and were included in this analysis. Importantly, evidence of hypertension with high-risk features was present in just over one-third of patients, suggesting that this was a common phenotype within the trial population. Notably, 60% of these patients were classified as high-risk because of left ventricular hypertrophy alone, highlighting the importance of hypertensive target-organ damage rather than blood pressure levels alone.

The key finding was a statistically significant interaction between treatment assignment and hypertension status. During a mean follow-up of 1.6 years, patients without high-risk hypertension features who received apixaban had approximately a 60% lower risk of recurrent ischemic stroke or systemic embolism compared with those receiving aspirin. In contrast, no benefit was observed among patients with high-risk hypertension features.

Overall, these findings generate an intriguing hypothesis: among patients with cryptogenic stroke and atrial cardiopathy, markers of severe hypertensive vascular disease may identify individuals less likely to benefit from anticoagulation. If confirmed, incorporating hypertension severity and target-organ damage into stroke mechanism classification could improve patient selection for future secondary prevention trials. For now, however, the results should be considered hypothesis-generating rather than practice changing.

To wrap up,

- When selecting an antihypertensive therapy, combination treatment is often more effective and better tolerated than escalating monotherapy.
- Isolated diastolic hypertension does not appear to modify the benefits of blood pressure lowering and should not be overlooked in clinical practice.

- Finally, in patients with cryptogenic stroke, markers of high risk features of hypertension may help to identify biologically distinct subgroups and refine future secondary prevention strategies.

Taken together, these studies suggest that the future of hypertension management lies not only in lowering blood pressure, but in understanding which treatment, for which patient, and for which underlying vascular phenotype.

Full references and links to all 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 Maria Magdalena Gabriel and editor-in-chief Linxin Li.

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