

Reply to Letter to the Editor: “Comments on Nonsustained Atrial Fibrillation and Stroke Risk: Methodological and Interpretive Considerations”

To the Editor,

We thank the authors¹ for their thoughtful comments on our article.²

First, we would like to clarify that the figure “163” in the first sentence of the Results section was a typographical error. The correct number of patients with NS-AF at inclusion was 133, and this has been corrected in the published version. After propensity score matching, 20 cases were excluded, yielding 113 patients in the NS-AF group and 113 controls for all subsequent analyses.

Regarding the authors’ questions:

In both the ASSERT and RATE trials, patients with cardiac devices were enrolled; these individuals had a higher risk of cardiovascular events and closer follow-up.^{3,4} In contrast, our cohort comprised symptomatic patients referred for palpitations, with visually adjudicated clinical AF episodes rather than device-detected atrial high-rate episodes. In those trials, AF was detected by device algorithms, which may sometimes be confused with atrial tachyarrhythmias. In our study, we did not consider regular rhythms as atrial fibrillation during Holter evaluation and excluded them from analysis. There are also notable differences between the study populations. The ASSERT trial included hypertensive patients aged ≥ 65 years, and aspirin use was around 60%, whereas in the RATE trial, approximately 15% of patients were receiving anticoagulant therapy. We acknowledge the limitations of 24-hour Holter monitoring and the potential underestimation of AF burden. Our patient population who documented episodes of an AF episode (even very short) in only 24-hour Holter monitoring is also quite different from the patient population who had short episodes of AF in continuous rhythm monitoring in the ASSERT and RATE registry. To be able to document AF in patients in only 24-hour Holter monitoring probably indicates that those patients either already had longer episodes of AF/higher AF load or would develop it.

In our study, all brief AF episodes were verified by 2 independent observers using 3-channel ECG recordings, and age was adjusted for in multivariable models, in which NS-AF remained an independent predictor of ischemic stroke. While extended monitoring and long-term prospective follow-up are indeed important, our primary aim was to highlight a common problem in everyday clinical practice, brief AF episodes detected on routine Holter monitoring, and to help clinicians avoid overlooking the increased stroke risk, particularly among patients with higher CHA₂DS₂-VA scores. Moreover, in previous studies, even the presence of short atrial runs on 48-hour Holter monitoring has been shown to be associated with an increased risk of stroke and adverse cardiovascular outcomes.⁵ For such individuals, closer follow-up and individualized risk assessment may be warranted. We did not claim that these patients never experienced longer episodes;

LETTER TO THE EDITOR REPLY

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Table 1. Independent Predictors of Ischemic Stroke in Multivariable Model Incorporating the CHA₂DS₂-VAsC Score

Variables	OR [Exp(B)]	95% CI (Lower–Upper)	P
eGFR	0.997	0.975-1.018	.752
Pulmonary artery systolic pressure	1.018	0.981-1.056	.357
Left atrium enlargement	0.978	0.872-1.097	.707
Left ventricle hypertrophy	1.920	0.755-4.881	.171
CHA ₂ DS ₂ -VAsC score	1.603	1.210-2.123	<.001
Paroxysmal atrial fibrillation	3.623	1.231-10.665	.019

eGFR, estimated glomerular filtration rate; NS-AF, non-sustained atrial fibrillation.

rather, our key message is that when short AF episodes are observed on Holter monitoring, clinicians should recognize the elevated stroke risk, especially when the CHA₂DS₂-VA score is ≥ 2 .

We used the CHA₂DS₂-VA score because the latest European Society of Cardiology guidelines recommend its use.⁶ The ASSERT trial applied the CHA₂DS₂-VAsC score, whereas the RATE trial used the CHA₂DS₂ score. To eliminate any confusion, we also reanalyzed our cohort using the CHA₂DS₂-VAsC score, and the independent predictive value of short AF episodes remained unchanged (Table 1).

We appreciate the opportunity to provide these clarifications and thank the reviewers for their valuable insights.

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