

Vericiguat in Experimental Atrial Fibrillation: Distinguishing Remodeling from Rhythm Control

To the Editor,

We read with great interest the experimental study by Zhang et al,¹ which examined the effects of vericiguat on atrial electrical and structural remodeling in a rat model of atrial fibrillation (AF). The authors demonstrated coherent antiremodeling signals, including reductions in left atrial enlargement, fibrosis, collagen I, and NT-proBNP, together with favorable changes in CaMKII, connexin 43, and autophagy-related proteins. These findings are biologically relevant. Nevertheless, the conclusion that vericiguat attenuates "AF progression" and the discussion of restored "electrophysiological stability" appear stronger than the rhythm and mechanistic endpoints directly assessed, raising 2 points that may refine interpretation of this important work.

First, the temporal relationship between rhythm assessment and vericiguat exposure deserves clarification. In the Methods and Results, AF frequency and duration were recorded during model establishment after ACh-CaCl₂ administration, and the 16 animals with AF were subsequently randomized to the AF and vericiguat groups. The reported frequency and duration values therefore appear to characterize the pre-treatment model rather than rhythm response after 4 weeks of vericiguat. No post-treatment AF burden, inducibility, atrial effective refractory period, action-potential duration, or conduction mapping is reported. Accordingly, normalization of CaMKII and connexin 43 supports molecular changes consistent with electrical remodeling, but it does not by itself demonstrate restoration of electrophysiological stability or reduction of AF burden. This distinction is particularly relevant because earlier work with vericiguat in a rabbit AF model incorporated direct electrophysiological endpoints, including atrial refractoriness and AF inducibility.² Demonstrating concordance between such functional endpoints and the molecular changes observed here would substantially strengthen the antiarrhythmic inference.

Second, the interpretation of autophagy merits similar caution. The endpoint pattern of increased ATG7 and LC3-II/I with reduced p62 in AF, and its reversal with vericiguat, is compatible with altered autophagy-related signaling. However, autophagy is a dynamic degradative process, and static measurements of LC3 and p62 cannot, by themselves, distinguish increased autophagosome formation from impaired downstream lysosomal clearance. Current methodological guidance therefore emphasizes assessment of autophagic flux using complementary approaches, such as lysosomal inhibition or suitable reporter systems.³ Moreover, because autophagy was not experimentally inhibited or genetically perturbed, the present data establish association rather than mediation between autophagy-related changes and the antifibrotic effects of vericiguat. Thus, "modulation of autophagy-related markers" may be a more proportionate mechanistic description than a demonstrated autophagy-mediated pathway.

We therefore view the study as providing a compelling preclinical signal that vericiguat attenuates atrial structural remodeling, while its direct antiarrhythmic and autophagy-mediated effects remain hypothesis-generating. Future

LETTER TO THE EDITOR

Hasan Burak İşleyen¹ 

Emirhan Hancıoğlu² 

Sevil Tuğrul Yavuz³ 

¹Department of Cardiology, Faculty of Medicine, Bezmialem Vakıf University, İstanbul, Türkiye

²Department of Cardiology, Acibadem District Hospital, İstanbul Medipol University, İstanbul, Türkiye

³Department of Cardiology, Başakşehir Çam and Sakura City Hospital, İstanbul, Türkiye

Corresponding author:

Emirhan Hancıoğlu
✉ hanciogluemir@gmail.com

Available Online Date: October 6, 2026

Cite this article as: İşleyen HB, Hancıoğlu E, Yavuz ST. Vericiguat in experimental atrial fibrillation: distinguishing remodeling from rhythm control. *Anatol J Cardiol*. 2026;XX(X):X-X.

DOI: 10.14744/AnatolJCardiol.2026.6998



Copyright©Author(s) - Available online at anatoljcardiol.com.
Content of this journal is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

experiments combining posttreatment continuous rhythm phenotyping or standardized AF inducibility with direct electrophysiological measurements and autophagic-flux assessment could connect the molecular findings to rhythm outcomes and more firmly establish the proposed mechanistic pathway.

Note: The authors of the relevant article were given the opportunity to reply, but they chose not to send a response.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

REFERENCES

1. Zhang X, Wang Y, Shen L, et al. Vericiguat alleviates atrial electrical and structural remodeling in rats with atrial fibrillation. *Anatol J Cardiol.* 2026;30(8):508-516. [\[CrossRef\]](#)
2. Lou Q, Li L, Liu G, et al. Vericiguat reduces electrical and structural remodeling in a rabbit model of atrial fibrillation. *J Cardio-vasc Pharmacol Ther.* 2023;28:10742484231185252. [\[CrossRef\]](#)
3. Klionsky DJ, Abdel-Aziz AK, Abdelfatah S, et al. Guidelines for the use and interpretation of assays for monitoring autophagy (4th edition). *Autophagy.* 2021;17(1):1-382. [\[CrossRef\]](#)