Letter to the Editor

Nonpermanent atrial fibrillation in the new European Society of Cardiology guidelines

La fibrilación auricular no permanente en la nueva guía de la Sociedad Europea de Cardiología

To the Editor,

A recent issue of *Revista Española de Cardiología* published comments by the Working Group of the Spanish Society of Cardiology[1] on the new atrial fibrillation (AF) guidelines of the European Society of Cardiology.[2]

These guidelines make only a few changes regarding anticoagulant therapy; however, biomarkers could aid decision-making in inconclusive cases where the patient has only 1 risk factor, as mentioned by the Working Group of the Spanish Society of Cardiology.

One change made in the guidelines is that the clinical pattern of arrythmia should not affect the thromboprophylaxis indication, which is listed as a class III recommendation, rather than as the class IIa recommendation included in the 2010 guidelines.[3] This recommendation is supported by a single reference published in 2000 and is based on the Stroke Prevention in Atrial Fibrillation (SPAF) studies,[4] in which the authors state verbatim in the limitations section that the risk of "stroke associated with intermittent AF is likely to be related to the frequency and duration of paroxysms... [which were] not accurately ascertained in this study."

In recent years, several articles have discussed the influence of AF pattern on thromboembolic risk, with most concluding that nonpermanent (mainly paroxysmal) AF carries a lower risk. The same conclusion was also supported by analyses of patient subgroups included in key studies on direct-acting anticoagulants.

In the ARISTOTLE trial[5] analysis, the yearly rate of stroke or systemic embolism in patients with paroxysmal AF, compared with persistent and permanent AF, was 0.98 vs 1.52 (hazard ratio [HR], 0.65; 95% confidence interval [95%CI], 0.48-0.87; $P = .003$).

In the ROCKET trial,[6] patients with paroxysmal AF had a significantly lower rate of stroke: 1.73 vs 2.18 (HR, 0.78; 95%CI, 0.61-0.99; $P = .045$).

In the ENGAGE trial,[7] the primary endpoint was reached less often in paroxysmal AF (1.49%/y) than persistent (1.83%/y) or permanent (1.95%/y) AF, with these differences being statistically significant.

However, although the event rate in these trials was lower in paroxysmal AF, it was still high enough to warrant anticoagulant therapy, even though we should keep in mind that these studies included high-risk patients.

Last, a relevant aspect in this topic is the design of the NAVIGATE[8] and RESPECT[9] trials. Both of these trials included patients with a history of stroke and compared rivaroxaban or dabigatran therapy with anticoagulant treatment. In both cases, prior monitoring was performed for at least 20 hours to rule out AF episodes longer than 6 minutes; in other words, the authors considered that patients with a history of stroke and AF lasting < 6 minutes could be treated with anticoagulants.

While we agree that thromboembolic prophylaxis should be determined by the thromboembolic risk profile rather than the clinical pattern of arrythmia, we believe that the available information means that the AF type can be considered in decision-making about inconclusive cases where the patient is not at high risk, with a level of evidence not inferior to the evidence level attributed to biomarkers.

FUNDING

This project has not received any funding.

AUTHORS' CONTRIBUTIONS

E. Vázquez Ruiz de Castroviejo: manuscript idea, design, and preparation. A. Linde Estrella, J.C. Fernández Guerrero, and F.M. García García: assistance with manuscript preparation.

CONFLICTS OF INTEREST

None.

Eduardo Vázquez Ruiz de Castroviejo,* Antonio Linde Estrella, Francisco Manuel García García, and Juan Carlos Fernández Guerrero

Unidad de gestión clínica de Cardiología, Complejo Hospitalario de Jaén, Jaén, Spain

*Corresponding author:
E-mail address: evrcastro@gmail.com
(E. Vázquez Ruiz de Castroviejo).

Available online 31 July 2021

https://doi.org/10.1016/j.rec.2021.07.004

SEE RELATED CONTENT:
http://doi.org/10.1016/j.rec.2020.11.023
http://doi.org/10.1016/j.rec.2021.10.004

REFERENCES

1. Grupo de Trabajo de la SEC para la guía ESC 2020 sobre el diagnóstico y tratamiento de la fibrilación auricular, Revisores expertos para la guía ESC 2020 sobre el diagnóstico y tratamiento de la fibrilación auricular y Comité de Guías de la SEC. Comentarios a la guía ESC/EACTS 2020 sobre el diagnóstico y tratamiento de la fibrilación auricular. *Rev Esp Cardiol*. 2021;74:378-383.
2. Hindricks G, Potpara T, Dagres N, et al.2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). *Eur Heart J*. 2021;42:373–498.
3. Camm AJ, Kirchhof P, Lip GYH, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J*. 2010;31:2369–2429.
4. Hart RG, Pearce LA, Rothbart RM, et al. Stroke with intermittent atrial fibrillation: incidence and predictors during aspirin therapy. Stroke Prevention in Atrial Fibrillation Investigators. *J Am Coll Cardiol*. 2000;35:183–187.

5. Al-Khatib SM, Thomas L, Wallentin L, et al. Outcomes of apixaban vs. warfarin by type and duration of atrial fibrillation: results from the ARISTOTLE trial. *Eur Heart J.* 2013;34:2464–2471.
6. Steinberg BA, Hellkamp AS, Lokhnygina Y, et al. Higher risk of death and stroke in patients with persistent vs. paroxysmal atrial fibrillation: results from the ROCKET-AF Trial. *Eur Heart J.* 2015;36:288–296.
7. Link MS, Giugliano RP, Ruff CT, et al. Stroke and mortality risk in patients with various patterns of atrial fibrillation: results from the ENGAGE AF-TIMI 48 trial. *Circ Arrhythm Electrophysiol.* 2016;10:e004267.
8. Hart RG, Sharma M, Mundl H, et al. Rivaroxaban for stroke prevention after embolic stroke of undetermined source. *N Engl J Med.* 2018;378:2191–2201.
9. Diener HC, Sacco RL, Easton JD, et al. Dabigatran for prevention of stroke after embolic stroke of undetermined source. *N Engl J Med.* 2019;380:1906–1917.

Nonpermanent atrial fibrillation in the new European Society of Cardiology guidelines. Response

La fibrilación auricular no permanente en la nueva guía de la Sociedad Europea de Cardiología. Respuesta

To the Editor,

We are grateful for the critical analysis by Vázquez Ruiz de Castroviejo et al., which raises the important question of thromboembolic risk stratification in patients with atrial fibrillation (AF). Analysis of arrhythmia burden is probably one of the most important factors of those which, in recent years, have entered clinical practice. The new AF guidelines also cover this concept, highlighting its relevance.[1,2]

However, we must also consider the limitations inherent to this approach. Firstly, the incidence of thromboembolic events in paroxysmal forms is significant, which is an argument for starting anticoagulant therapy independently of whether it shows a greater benefit in other forms of the disease. No study to date has demonstrated that a thromboembolic risk-prevention strategy guided by AF classification pattern improves the risk profile, therapeutic benefit or safety of anticoagulant therapy. Recent cautious attempts observed no benefit from anticoagulant treatment guided by individual patients' arrhythmia burden at any time.[3] Nonetheless, each patient's arrhythmia burden is directly related to their cardiovascular and thromboembolic risk profile. Therefore, any attempt to differentiate the therapeutic benefits of anticoagulant treatment should involve a combined analysis of the arrhythmia burden and the profile of cardiovascular risk factors. Their independence has not been demonstrated in prospective studies, and AF holds increasing weight as a marker of risk, in conflict or accordance with its nature as a primary causative factor.[1]

We disagree about the supposed lack of advances in anticoagulant treatment; these have been substantial in terms of the consolidation of direct-acting anticoagulants as a preferred treatment,[1] but we agree with Vázquez Ruiz de Castroviejo et al. that the arrhythmia burden will, in the near future, become a key factor in embolic risk stratification. Although the available evidence at present does not allow its translation to management, it certainly ensures this this important area of clinical research remains active.

FUNDING

No funding received.

AUTHORS' CONTRIBUTIONS

D. Calvo and E. Arbelo contributed equally to the writing and review of this manuscript. Both have approved the final version and accept responsibility for the content.

CONFLICTS OF INTEREST

No conflicts of interest.

David Calvo[a,b,*] and Elena Arbelo[a,b]

[a]*Grupo de Trabajo de la SEC para la guía ESC 2020 sobre el diagnóstico y tratamiento de la fibrilación auricular*
[b]*Comité de Guías de la Sociedad Española de Cardiología*

[*] Corresponding author:
E-mail address: dcalvo307@secardiologia.es (D. Calvo).

Available online 12 November 2021

https://doi.org/10.1016/j.rec.2021.10.004

SEE RELATED CONTENT:
http://doi.org/10.1016/j.rec.2021.07.004

REFERENCES

1. Hindricks G, Potpara T, Dagres N, et al.2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). *Eur Heart J.* 2021;42:373–498.
2. Grupo de Trabajo de la SEC para la guía ESC 2020 sobre el diagnóstico y tratamiento de la fibrilación auricular, Revisores expertos para la guía ESC 2020 sobre el diagnóstico y tratamiento de la fibrilación auricular y Comité de Guías de la SEC. Comentarios a la guía ESC/EACTS 2020 sobre el diagnóstico y tratamiento de la fibrilación auricular. *Rev Esp Cardiol.* 2021;74:378-8310.
3. Martin DT, Bersohn MM, Waldo AL, et al. Randomized trial of atrial arrhythmia monitoring to guide anticoagulation in patients with implanted defibrillator and cardiac resynchronization devices. *Eur Heart J.* 2015;36:1660–1668.