

**Degree of Anticoagulation Control in Patients With Atrial Fibrillation in Spain: Need to Minimize Biases and Contextualize Results.**  
Response by Anguita Sánchez et al.



**Grado de control de la anticoagulación en pacientes con fibrilación auricular en España: necesidad de minimizar sesgos y contextualizar resultados. Respuesta de Anguita Sánchez et al.**

**To the Editor,**

We have carefully read the comments of Alfaro-Lara et al. on the results of our study CALIFA,<sup>1</sup> as well as on those of the PAULA<sup>2</sup> and ANFAGAL<sup>3</sup> studies. These studies provided information on the quality of anticoagulation with vitamin K antagonists in Spain and in patients with nonvalvular atrial fibrillation in the “real-life” setting. The 3 studies agreed that about 40% to 50% of these patients had a time in therapeutic range (TTR) < 65% in the 6 to 12 months prior to the analysis, that is, that they lacked adequate anticoagulation. This datum would be even worse if the recommendations of the European Society of Cardiology were being followed, which establishes a TTR > 70% as a criterion of good control with vitamin K antagonists.<sup>4</sup> These results are in accordance with those of another Spanish study also published in 2015, the FANTASIIA study.<sup>5</sup> This study found an even higher percentage (54%) of “poorly” anticoagulated patients (TTR < 65% by the Rosendaal method).

Alfaro-Lara et al. point out that these studies, with the exception of ANFAGAL (which largely randomly selected patients and investigators), may provide biased estimates due to the nonrandomized selection of investigators and the consecutive, nonrandomized, inclusion of the patients; we agree with this comment and discussed this aspect as a limitation in our study. However, most real-life registries of various diseases share this or a similar bias, without diminishing their results. Their veracity is particularly evident when the results are consistent across all studies, as is the case here, with similar results obtained in an even more methodologically correct study such as ANFAGAL. Alfaro-Lara et al. also note that the TTR (TTR percentage) of these studies (69% and 63.8% by the Rosendaal method) are similar to or even better than those found in other countries, with which we agree. However, they are always inferior to those of Australian and Northern European studies, where the TTR exceeds 70%,<sup>6</sup> as in some Spanish centers.<sup>7</sup> In the latter study, conducted in Murcia, Spain, the TTR reached 79.7% in patients with a SAME-TT2R2 score of 0 and even reached 72.3% in patients with a SAME-TT2R2 score of 5. These findings indicate that vitamin K antagonists can achieve better quality anticoagulation than usually obtained. Moreover, to us, it seems more important that the simple TTR value—the percentage of patients with a low TTR (< 65%)—lies between 40% and 54% in these 3 Spanish registries. It also seems arbitrary to argue, as Alfaro-Lara et al. have done, that the TTRs are better if an INR (International Normalized Ratio) range between 1.8 and 3.2 is considered adequate. And why not consider a range

between 1.7 and 3.5 to be “adequate”? We believe that we should be strict and adhere to the recommendations of the clinical practice guidelines, which define an INR between 2 and 3 to be appropriate, and even believe that the TTR of a patient should be increased to > 70% to be considered adequate. Unfortunately, even with the above qualifications, we believe that our conclusion—that patients with nonvalvular atrial fibrillation who receive vitamin K antagonists in Spain are poorly controlled—is sound.

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Response by Barrios et al



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**To the Editor,**

After a careful reading of the letter by Alfaro-Lara et al., we would like to make a number of comments. First, several studies have analyzed the degree of control of the international normalized ratio (INR) in patients with atrial fibrillation receiving anticoagulation therapy with vitamin K antagonists in Spain. Although each study has its own particular methodology, all have shown similar results, namely, that in clinical practice about 35% to 45% of patients receiving vitamin K antagonists have poor control