Letter to the Editor

Anticoagulation Treatment in Patients with Atrial Fibrillation and Results of the RAFTING study

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We read with interest the article entitled "Clinical Profile and Therapeutic Management of Patients with Atrial Fibrillation in Greece: Results from the Registry of Atrial Fibrillation to investigate New Guidelines (RAFTING)", which was published in a recent issue of the Hellenic Journal of Cardiology. As reported in the paper, the purpose was: "projecting a national strategy to improve management of patients with atrial fibrillation".[1] However, we believe that the purpose was not fulfilled, in view of both the poor quality of the results and the unjustified comments provided by the authors in their Discussion section. Our concerns could be summarized by the following points:

1. The study included only patients in hospital emergency departments, which in any case cannot be a representative sample of all patients with atrial fibrillation at a national level, as claimed by the authors.
2. Patients treated with warfarin reported international normalized ratio (INR) values in the therapeutic range (2-3) in 60% of cases in the most recent pre-hospital measurement; thus, the low rate of 34% during hospitalization can be attributed to other factors, occurring either immediately before or after admission.
3. Therefore, these findings cannot be "a strong argument for the use of new anticoagulants such as dabigatran, rivaroxaban or apixaban, the use of which do not require laboratory monitoring", as the authors claimed. This argument can also be considered as unwarranted because, according to recent recommendations of the European Society of Cardiology, the new drugs require blood tests as well, close medical supervision and very disciplined patients, while they are affected by the co-administration of many other drugs. As emphasized repeatedly, "strict therapy compliance by the patient is crucial!". It is also stated that the new drugs "have not been assessed in terms of compliance" and "there are unsolved problems for their optimal use".[2]
4. Apart from all these methodological remarks, it is demeaning and unfair to Greek cardiologists, who make up a proportionately large population by world standards, to conclude that they succeed in adjusting INR in only 34% of patients, while in northern Europe the rates are up to 76%.[3] On the contrary, the impression is that Greek patients are treated better than patients in clinical studies, where the old compared to the novel anticoagulants have demonstrated marginal differences in efficacy and safety.

5. The final suggestion of RAFTING, that claims a need for full compliance with the guidelines, is indefinite and contrasts with the initial purpose supporting "the development of a national strategy", since "every country has specific characteristics and data applicable in one country do not apply to others". Moreover, according to current guidelines, old and new anticoagulants are in the same recommendation category, IA. RAFTING completely ignored the current financial and social characteristic of Greek patients, as well as the still ongoing bankruptcy of the National Health Care System. Instead, no statement to encourage optimal anticoagulation in those receiving warfarin was provided.
6. Preliminary data from a European registry, in the richest countries, (PREFER in AF), indicate that only 6% of patients with atrial fibrillation are treated with the new anticoagulants.[4] Given that the most important factor in patient compliance is the cost, we can appreciate what the consequences for the Greek patients would be, if we replaced a very good and inexpensive drug with a very expensive one, whose interruption for even a few days can have tragic consequences. The National School of Public Health has already estimated that one third of patients either discontinue therapy for financial reasons or decrease food and heating costs in order to acquire them.
7. We strongly believe in a "national strategy"; however, our patriotic and above all our medical duty to our patients, in this dark period in our country, is to prescribe and regulate them with the old well established drugs. As for the "novel anticoagulants", which in clinical trials have been administered free of charge, we can wait some time for them to prove their value in clinical practice and by then, hopefully, we will be able to provide them to our patients without tragic consequences.

Finally, while it is noted that the above study was funded by a pharmaceutical company producing a new anticoagulant, the individual financial relationships of the authors are not clarified. Neither of the authors of this Letter has any conflict of interest in this regard.

References

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The authors reply

We thank Drs. Ntellos and Thomopoulos for their interest in our work and their letter, which indeed brings up some important issues.

Previous epidemiological studies on atrial fibrillation (AF) in Greece were small and/or confined to certain geographical areas. Thus, the purpose of the RAFTING registry was to provide updated and country-wide epidemiological evidence for AF. For this reason, the study was carefully designed to provide data as representative as possible. First, RAFTING recruited a large number of patients (n=1127). Second, those patients were recruited by a large number of centers (n=31) covering all regions of the country. Third, to avoid over- or under-representation of certain regions, each center recruited a pre-specified number of patients defined according to the distribution of the population in Greece, as outlined by the latest national census. Finally, the recruitment of patients in each center was consecutive and was not restricted to patients attending cardiology departments or clinics, but comprised all patients with AF or AF history who visited the emergency department, regardless of the reason for the visit. These properties render RAFTING the hitherto most representative study of AF in Greece and one of the most representative AF registries in the literature.

The low prevalence of within-therapeutic-range INR values is a widely encountered problem stressed

by several studies and registries in the literature. We do not claim that this is a reason to prescribe the new oral anticoagulants (NOACs), but that it is an existing problem that needs to be addressed and taken under consideration when designing health strategies. Recognizing the actual situation regarding INR compliance is not an offence to practicing cardiologists, but rather a good starting point for attempting improvement. It should be noted that, even in clinical trials, Greek participating hospitals achieved INR values within the therapeutic range in 50% of cases.

As regards NOACs, the study was performed before these drugs were licensed for stroke prevention in AF and thus no data for their use were collected or provided. The issue of NOACs was obviously beyond the scope of RAFTING; thus we cited them only in a single phrase at the end of the Discussion and we did not recommended them at all for stroke prevention in AF, as Ntellos and Thomopoulos claim. More importantly, our data are still very valuable as a basis for reducing, for example, the number of patients who against all evidence still receive clopidogrel, or who do not receive antivitamin-K, despite a high risk.

The issue of the cost of AF therapies is indeed a very important one, but RAFTING was not designed to provide cost analysis data and therefore this issue was also beyond the scope of the study.

Finally, RAFTING was designed and carried out by the Hellenic Cardiological Society. A pharmaceutical company did fund the study, as clearly disclosed in the paper, but it was not involved in the interpretation of data or the writing of the paper.

Dimitrios Farmakis, Athanasios Pipilis
on behalf of the RAFTING Investigators