Relationship between Mediterranean diet and time in therapeutic range in atrial fibrillation patients taking vitamin K antagonists

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Aims
It is unclear if atrial fibrillation (AF) patients treated with oral vitamin K antagonists (VKAs) must follow a specific diet to avoid interference with anticoagulation. The aim of this study was to assess if Mediterranean diet (Med-Diet) may affect quality of anticoagulation, as expressed by the time in therapeutic range (TTR).

Methods and results
A prospective observational study including 553 non-valvular AF patients. Time in therapeutic range was calculated for all patients treated with VKAs, and adherence to Med-Diet was evaluated with a validated nine-item dietary questionnaire. Cardiovascular events (CVEs), such as cardiovascular death and fatal/non-fatal stroke or myocardial infarction, and bleedings were recorded. The median follow-up was 31.6 months. The median number of international normalized ratios for each patient was 63.0 (35.0–98.0) and 38 730 blood samples were analysed. In the whole cohort, the mean TTR was 65.5 ± 17.8%. The mean Med-Diet score was 5.19 ± 1.6, with frequent use of olive oil (90.1%), fruits (88.4%), and vegetables (69.3%) and low meat intake (71.2%). There were no differences among tertiles of Med-Diet score regarding TTR. A multivariable linear regression analysis showed that diabetes (β: −0.105, \( P = 0.015 \)) and the use of angiotensin converting enzyme inhibitor/angiotensin receptor blockers (β: 0.153, \( P < 0.001 \)) were associated with TTR. Compared with those without, AF patients with a CVE had significantly lower TTR (65.9 ± 17.9 vs. 59.6 ± 15.9, \( P = 0.029 \)) and Med-Diet score (5.2 ± 1.5 vs. 4.4 ± 1.9, \( P = 0.004 \)). A reduction of CVE was observed for each point of the Med-Diet score (hazard ratio 0.790, \( P = 0.017 \)).

Conclusion
In our cohort of AF patients, Med-Diet is not associated with changes in TTR, and thus can be recommended for AF patients who are taking VKAs.

Keywords
Atrial fibrillation • Mediterranean diet • Time in therapeutic range • Vitamin K • Food–drug interaction • Cardiovascular events

Introduction
In patients with atrial fibrillation (AF) taking vitamin K antagonists (VKAs), recorded international normalized ratio (INR) values outside the therapeutic range of 2.0–3.0, as reflected by the average individual time in therapeutic range (TTR), are still common despite major efforts from healthcare providers to adjust drug dosages and educate patients. This represents an important
What’s new?

- The common belief is that the intake of some foods rich of vitamin K, such as leafy greens vegetables, may interfere with anticoagulation.
- As Med-Diet is rich in fruits and vegetables, we analysed if adherence to Med-Diet had a negative impact on the TTR in 553 patients with AF on treatment with VKAs.
- The study demonstrates that adherence to Med-Diet was not associated with changes in TTR, so suggesting that a food rich in fruits and vegetables actually does not interfere with anticoagulation by VKAs.
- An important clinical implication of this finding is that Med-Diet could represent a dietary option for AF patients on treatment with VKAs.

Clinical challenge, since TTR inversely correlates with thrombosis, mortality, and bleeding. Thus, VKAs are underused in clinical practice because of physicians’ fear of erratic anticoagulation control and increased risk of bleeding, especially in the elderly.

Educational advice and counselling is often given to AF patients starting VKAs, in order to improve adherence of patients to treatment and to enhance anticoagulation stability and better TTRs, and a great emphasis is still made on diet and nutritional information.

There are few (and often inconclusive) studies investigating the influence of dietary habits on the anticoagulation quality, and guidelines still do not provide sufficient indication about the more appropriate dietary approaches to maintain a good TTR in VKA-anticoagulated AF patients. Particular attention has been classically focused on vitamin K-rich foods, such as dark-green leafy vegetables, which could interfere with VKA anticoagulation stability. The Mediterranean diet (Med-Diet) is characterized by a high intake of vitamin K-rich foods, such as green vegetables, and therefore, could represent a unique tool to establish if a diet rich in fruits and vegetables may interfere with TTR. Thus far, the interplay between Med-Diet adherence and TTR in AF patients has never previously been examined.

In the present study, we report for the first time the results of a prospective study evaluating the relationship between adherence to Med-Diet and TTR in a large AF population on chronic VKA treatment.

Methods

In this prospective, single-centre, observational cohort study, we consecutively recruited 600 AF patients receiving oral anticoagulants from I Medical Clinic, Atherothrombosis Center of Sapienza University of Rome, where patients are followed for the monitoring of INR and VKA dosage, from February 2008 to October 2013. All patients with non-valvular AF, aged ≥18 years were included in the study. All patients were treated with VKA (warfarin/acenocoumarol) after appropriate risk stratification according to the CHA2DS2-VASc score (and previously according to CHADS2 Score).

Exclusion criteria: mechanical or biologic prosthetic valves, severe valvulopathies, congenital heart diseases, severe cognitive impairment (e.g. Alzheimer’s disease, Parkinson’s disease), and chronic inflammatory diseases. Furthermore, we excluded subjects with active neoplastic diseases, liver cirrhosis, or if they were taking any vitamin or antioxidant supplementation.

The presence of cardiovascular risk factors, such as arterial hypertension, diabetes and heart failure (HF), was assessed using international definitions, as previously described.

Adherence to Mediterranean diet

Adherence to the Med-Diet was investigated by administration of a short dietary questionnaire that was elaborated by Martinez-Gonzalez et al. and was assessed using a validated food-frequency questionnaire with 136 items. This short questionnaire included the following: (i) olive oil (≥1 spoon/day); (ii) fruit (≥1 serving/day); (iii) vegetables or salad (≥1 serving/day); (iv) both fruit (≥1 serving/day) and vegetables (≥1 serving/day); (v) legumes (≥2 servings/week); (vi) fish (≥3 servings/week); (vii) wine (≥1 glass/day); (viii) meat (<1 serving/day); (ix) white bread (<1/week) or whole-grain bread (>5/week).

Follow-up visits were scheduled every 2–4 weeks for INR monitoring (therapeutic range of 2.0–3.0). Patients were asked to report to physician every change in dietary and medications. If a hospitalization occurred during the follow-up, the patient was required to submit medical documentation or copies of medical records.

Main outcome

Main outcome of the study was to analyse in AF patients, the quality of anticoagulation control, as assessed by TTR, in relation to the adherence to Med-Diet. Specifically, TTR was calculated with the method described by Rosendaal et al. which uses linear interpolation of INR values to assign to each follow-up day a value of INR. Then, the percentage of days that the INR was in the therapeutic range was calculated for each patient.

Events during the follow-up

Definition and adjudication of cardiovascular and cerebrovascular events have been previously described. Bleeding events were classified according to the ISTH criteria, as previously reported.

Statistical analysis

Categorical variables were reported as counts (percentage) and continuous variables as means ± standard deviation (SD) unless otherwise indicated. Independence of categorical variables was tested by χ2 test. Normal distribution of parameters was assessed by Kolmogorov–Smirnov test. Student’s unpaired t-test and Pearson product-moment correlation analysis were used for normally distributed continuous variables. Appropriate non-parametric tests (Mann–Whitney U test and Spearman rank correlation test) were employed for all the other variables. For the analyses we divided the entire population according to tertiles of the total Med-Diet score obtained from the nine-item questionnaire: first tertile 0–4 points, second tertile 5 points, third tertile 6–9 points. Stepwise multivariable linear regression analysis was used to assess factors influencing TTR. Only P values <0.05 were considered as statistically significant. All tests were two-tailed and analyses were performed using computer software packages (SPSS-180, SPSS Inc.).

Written informed consent was obtained from all subjects. The study was approved by the local Ethics Committee of Sapienza University,
and was conducted in accordance with the principles embodied in the Declaration of Helsinki.

**Results**

Of 600 screened patients, 18 were excluded from the analysis as follows: 6 because of active cancer, 8 for the presence of mechanical heart valve, 3 for severe cognitive impairment, and 1 for autoimmune disease. In addition, 5 patients refused to be included and 24 patients who were receiving supplements were excluded. Thus, 553 patients participated in the study. The median follow-up was 31.6 (15.1–47.6) months, yielding 1513 patient/years of observation. Clinical characteristics of AF population are reported in Table 1. Patients with AF had a clinical history complicated by myocardial infarction (MI)/cardiac revascularization in 20.3% and by ischaemic stroke/transient ischaemic attack (TIA) in 14.5%. Among the atherosclerotic risk factors, hypertension was detected in 87.5% and diabetes in 19.2%. The mean CHA2DS2-VASc score was 3.4 ± 1.5 in the entire population. In 10.8%, aspirin was combined with VKAs.

**Anticoagulation quality**

The median number of INR tests for each patient was 63.0 (interquartile range 35.0–98.0); mean days between two controls were 18.9 ± 7.1 days. Thus, 38730 blood samples were analysed to obtain INR values.

In the whole cohort, the mean TTR was 65.5 ± 17.8% (Table 1). Among AF patients, 357 (64.6%) were receiving warfarin, and 196 (35.4%) were acenocumarol.

**Mediterranean diet adherence and time in therapeutic range**

In the entire population, the mean total Med-Diet score was 5.19 ± 1.6. Based on single element consumptions, AF patients had a frequent use of olive oil (90.1%), fruits (88.4%), and vegetables (69.3%), while intake of meat was low (71.2%) had <1 serving/day (Table 2). None of the individual diet components was related to mean TTR.

During the follow-up, the Med-Diet questionnaire was administered a second time to check changes in the adherence to Med-Diet. The questionnaire was administered at a median time of 44.0 (29.0–60.0) months from baseline. In four patients, cardiovascular death occurred before the second administration of the questionnaire. Adherence to the Med-Diet decreased during the follow-up (from 5.19 ± 1.6 to 4.93 ± 1.5, \( P < 0.001 \)), but the Med-Diet score remained not correlated with TTR (\( R = 0.028, P = 0.508 \)).

### Table 1 Baseline characteristics of the study cohort

|                          | Overall (n = 553) | First tertile of Med-Diet 0–4 points (n = 165) | Second tertile of Med-Diet 5 points (n = 144) | Third tertile of Med-Diet 6–9 points (n = 244) | \( P^* \)  
|--------------------------|-------------------|---------------------------------------------|---------------------------------------------|---------------------------------------------|---------  
| Age (years)              | 72.9 ± 8.3        | 72.5 ± 9.0                                  | 72.7 ± 9.3                                  | 73.3 ± 7.0                                  | 0.590    
| Gender (females) (%)     | 40.0              | 42.4                                        | 44.4                                        | 35.7                                        | 0.173    
| Body mass index (kg/m²)  | 27.3 ± 4.3        | 27.3 ± 4.8                                  | 27.8 ± 4.2                                  | 26.9 ± 4.0                                  | 0.121    
| CHA2DS2-VASc score       | 3.4 ± 1.5         | 3.5 ± 1.6                                   | 3.3 ± 1.4                                   | 3.4 ± 1.5                                   | 0.405    
| Time in therapeutic range| 65.5 ± 17.8       | 63.6 ± 16.5                                 | 67.4 ± 18.6                                 | 65.7 ± 18.2                                 | 0.172    
| Mean week dosage of warfarin (mg) | 26.0 ± 11.7 | 26.7 ± 10.6                                 | 26.0 ± 13.5                                 | 25.7 ± 11.0                                 | 0.812    
| Mean week dosage of acenocumarol (mg) | 14.7 ± 6.5 | 13.0 ± 5.4                                  | 16.6 ± 6.4                                  | 15.0 ± 7.0                                  | 0.022**  
| Number of INR analysis, n | 63.0 (35.0–98.0) | 74.0 (44.5–104.0)                           | 55.5 (32.2–92.5)                            | 64.0 (35.0–98.7)                            | 0.037***  
| Mean days between two controls (days) | 18.9 ± 7.1 | 19.1 ± 8.0                                  | 19.0 ± 6.3                                  | 18.6 ± 7.0                                  | 0.716    
| Past medical history     |                  |                                            |                                            |                                            |          
| Arterial hypertension (%)| 87.5              | 87.3                                        | 89.5                                        | 86.5                                        | 0.680    
| Diabetes (%)             | 19.2              | 20.6                                        | 18.2                                        | 18.9                                        | 0.850    
| History of stroke/TIA (%)| 14.5              | 18.8                                        | 13.3                                        | 12.3                                        | 0.167    
| Heart failure (%)        | 14.3              | 17.6                                        | 9.1                                         | 15.2                                        | 0.092    
| History of MI/CHD (%)    | 20.3              | 21.2                                        | 16.8                                        | 21.7                                        | 0.476    
| Number of drugs, n       | 5.8 ± 2.4         | 5.7 ± 2.4                                   | 5.7 ± 2.5                                   | 5.9 ± 2.3                                   | 0.824    
| Anti-platelet therapy (%)| 10.8              | 7.9                                         | 11.8                                        | 12.3                                        | 0.349    
| ACE inhibitors/ARBs (%)  | 73.6              | 70.7                                        | 74.3                                        | 75.3                                        | 0.582    
| β-Blockers (%)           | 42.1              | 42.7                                        | 39.7                                        | 43.0                                        | 0.812    
| Ca-antagonists (%)       | 33.8              | 36.6                                        | 30.9                                        | 33.6                                        | 0.580    
| Amiodarone (%)           | 30.7              | 30.1                                        | 33.1                                        | 29.8                                        | 0.784    

Med-Diet, Mediterranean diet; TIA, transient ischaemic attack; MI, myocardial infarction; CHD, coronary heart disease; ACE, angiotensin converting enzyme; ARBs, angiotensin receptor blockers.

*ANOVA.

**First tertile vs. second and third, \( P = 0.016 \).

***First tertile vs. second and third, \( P = 0.029 \).
Regarding TTR and most clinical characteristics of AF patients with anticoagulation therapy, we found a significant increase of acenocoumarol dosage between the first and the other tertiles but the increase was not linear (Table 1). While there was no difference of warfarin dosage among tertiles of the Med-Diet score (Table 1), we divided our AF population according to tertiles of TTR (Table 1). There were no significant differences among Med-Diet tertiles in terms of any bleeding event (5.5% vs. 5.1%, P = 0.137), or those with or without a major bleeding (5.5±1.8 vs. 5.2±1.6, P = 0.277).

### Table 2 Food frequencies and mean TTRs according to the consumption different food components of the Med-Diet

<table>
<thead>
<tr>
<th>Consumption (Consumptions (%)</th>
<th>Mean TTR (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>1. Olive oil (≥ 1 spoon/day)</td>
<td>90.1</td>
<td>65.6 ± 18.0</td>
</tr>
<tr>
<td>2. Fruit (≥ 1 serving/day)</td>
<td>88.4</td>
<td>66.0 ± 18.0</td>
</tr>
<tr>
<td>3. Vegetables or salad (≥ 1 serving/day)</td>
<td>69.3</td>
<td>65.5 ± 18.4</td>
</tr>
<tr>
<td>4. Fruits (≥ 1 serving/day) and vegetables (≥ 1 serving/day)</td>
<td>67.1</td>
<td>65.6 ± 18.5</td>
</tr>
<tr>
<td>5. Legumes (≥ 2 servings/week)</td>
<td>40.7</td>
<td>66.2 ± 17.6</td>
</tr>
<tr>
<td>6. Fish (≥ 3 servings/week)</td>
<td>17.9</td>
<td>66.1 ± 18.5</td>
</tr>
<tr>
<td>7. Wine (≥ 1 glass/day)</td>
<td>36.0</td>
<td>65.6 ± 17.2</td>
</tr>
<tr>
<td>8. Meat (&lt; 1 serving/day)</td>
<td>71.2</td>
<td>66.3 ± 17.9</td>
</tr>
<tr>
<td>9. [White bread (&lt; 1/day) and rice (&lt; 1/week)] or whole-grain bread (&gt;5/week)</td>
<td>38.0</td>
<td>66.8 ± 17.6</td>
</tr>
</tbody>
</table>

To further investigate the relationship between adherence to Med-Diet and TTR, we divided our AF population according to tertiles of the Med-Diet score (Table 1). There were no significant differences among Med-Diet tertiles regarding TTR and most clinical characteristics of AF patients with the exception of obesity (Table 1). There was significant lower number of INR analyses observed in patients in the second and third tertile of Med-Diet, compared with the first tertile (Table 1). While there was no difference of warfarin dosage among tertiles of Med-Diet adherence, we found a significant increase of acenocoumarol dosage between the first and the other tertiles but the increase was not linear (Table 1).

### Table 3 Mean TTR according to the presence of selected variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean TTR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (female)</td>
<td>65.8 ± 18.2</td>
<td>65.3 ± 17.6</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>66.1 ± 17.9</td>
<td>62.0 ± 16.6</td>
</tr>
<tr>
<td>Diabetes</td>
<td>62.1 ± 16.7</td>
<td>64.4 ± 17.9</td>
</tr>
<tr>
<td>History of stroke/TIA</td>
<td>64.3 ± 18.5</td>
<td>65.8 ± 17.7</td>
</tr>
<tr>
<td>HF</td>
<td>62.8 ± 18.7</td>
<td>66.0 ± 17.6</td>
</tr>
<tr>
<td>History of MI/CHD</td>
<td>62.8 ± 16.9</td>
<td>66.3 ± 17.9</td>
</tr>
<tr>
<td>Anti-platelet therapy</td>
<td>65.2 ± 17.9</td>
<td>65.8 ± 17.7</td>
</tr>
<tr>
<td>ACE inhibitors/ARBs</td>
<td>67.2 ± 17.5</td>
<td>61.5 ± 17.4</td>
</tr>
<tr>
<td>β-Blockers</td>
<td>64.3 ± 17.8</td>
<td>66.8 ± 17.6</td>
</tr>
<tr>
<td>Ca-antagonists</td>
<td>66.7 ± 17.8</td>
<td>65.2 ± 17.6</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>65.5 ± 18.3</td>
<td>66.2 ± 16.2</td>
</tr>
</tbody>
</table>

HF, heart failure; TIA, transient ischaemic attack; MI, myocardial infarction; CHD, coronary heart disease; ACE, angiotensin converting enzyme; ARBs, angiotensin receptor blockers.

### Correlations and multivariate analysis

Univariate analysis of the factors potentially associated with TTR (Table 3), revealed that diabetes influenced negatively TTR, while the use of angiotensin converting enzyme (ACE) inhibitors/angiotensin receptor blockers (ARBs) was associated with a better TTR.

In a stepwise multivariable linear regression analysis, diabetes (β: −0.105, P = 0.015) and the use of ACE inhibitor/ARBs (β: 0.153, P < 0.001) were independently associated with TTR, after adjustment for gender (female), arterial hypertension, body mass index, history of stroke/TIA, HF, history of MI/coronary heart disease (CHD), anti-platelet therapy, β-blockers, Ca-antagonists, amiodarone, and total Med-Diet score. Same results were obtained in a model including single foods instead of Med-Diet score (data not shown).

### Ischaemic events

An ischaemic cerebro/cardiovascular event (CVE) occurred in 36 patients during the follow-up (2.36%/year): 7 fatal/non-fatal ischaemic stroke, 13 cardiac revascularization, 8 cardiovascular deaths, and 8 fatal/non-fatal MI. Patients experiencing a CVE had significantly lower TTR compared with those without (59.6±15.9 vs. 65.9±17.9, P = 0.029). In addition, Med-Diet score was significantly lower in patients with CVE compared with patients free from events (4.4±1.9 vs. 5.2±1.5, P = 0.004). In particular, a reduction of the risk of CVE was observed for each point of the Med-Diet score [hazard ratio: 0.790 (95% confidence interval, 0.651–0.958), P = 0.017].

### Bleeding events

During the follow-up, 116 bleedings were registered (7.7%/year): 30 major (7 cerebral/subdural, 7 gastrointestinal, 4 articular, 5 ocular, 3 haematuria, and 4 muscular) and 86 minor haemorrhages.

Similar TTRs were detected in patients without bleeding (65.0±18.2%) vs. those with minor (66.7±16.8%) or major (69.4±14.0%) bleeding (P = 0.356 among groups). There was no difference regarding Med-Diet adherence score between patients with and without any bleeding event (5.4±1.7 vs. 5.1±1.6, P = 0.137), or those with or without a major bleeding (5.5±1.8 vs. 5.2±1.6, P = 0.277).

### Discussion

In this prospective study, we show for the first time that in AF patients Med-Diet has a neutral effect on anticoagulation stability.
Food interactions with the VKAs are a matter of concern as fluctuation in dietary intake of vitamin K may influence the anticoagulant response to these drugs. Nevertheless, this interaction has been substantially demonstrated only in patients using specific supplements or herbal infusions. In addition, small studies have evaluated the role of specific vitamin K-rich aliments, but papers reporting the impact of a complete nutritional profile on the quality of anticoagulation control are limited and show equivocal results. One case-control study on 302 outpatients and 300 matched controls found that vitamin K, fat, carbohydrates, and fibre intake did not significantly affect anticoagulation response. In a Brazilian group of patients with vascular disease, however, an association between dietary habits, in particular the use of kidney beans, and anticoagulation instability was reported.

To the best of our knowledge, this is the largest study that examined the effect of a population-based diet on the quality of anticoagulation control in AF patients on chronic VKA treatment. We investigated the relationship between adherence to Med-Diet and TTR overall because this diet is based on ingestion of aliments, such as fruits and green vegetables, which may be rich in vitamin K and could theoretically interfere with TTR.

The novel finding of the present study is the lack of Med-Diet food interactions with anticoagulation stability, as no significant differences in TTR were detected among tertiles of Med-Diet. Of note, AF patients who poorly adhered to Med-Diet were more frequently checked for INR values during the follow-up. Even if this should not affect the TTR computation, the frequent INR monitoring may be independent from inadequate anticoagulation and simply reflect an individual need for frequent monitoring. Also, patients adhering less to Med-Diet apparently need less acenocumarol compared with the those who adhere more; however, we cannot exclude that this is a play of chance as no difference of warfarin dosage was detected among the tertiles of Med-Diet adherence. This finding needs to be further investigated and interpreted with an interventional trial.

In our study, there was a good average TTR in patients in the highest tertile of Med-Diet, which is characterized by high intake of fruits and vegetables, suggesting that the aliments assumed with the Med-Diet contain a vitamin K amount that does not affect the anticoagulant response to VKA.

A possible interpretation of this apparent paradox is that Med-Diet is rich of vitamin E, particularly in some of its components such as extra virgin olive oil. Thus, vitamin E seems to exert an anticoagulant effect by inhibiting the gamma-carboxylation of vitamin K-dependent clotting factors. In this context, it is worth noting that in AF anticoagulated patients, we previously demonstrated that serum levels of vitamin E linearly increase with Med-Diet adherence, and are associated inversely with ischaemic events, and directly with bleeding events. It may be possible, therefore, that in the Med-Diet the pro-coagulant effect of aliments rich in vitamin K, which gamma-carboxylates vitamin K-dependent factors, may be counterbalanced by its high vitamin E content.

Previous data from the ROCKET trial showed that diabetes, CHD, or HF were negatively associated with TTR. While we confirm the negative association between diabetes and TTR, only a trend for a lower TTR in patients with a clinical history of CHD or HF was detected.

An unexpected finding was the positive association between ACE inhibitors/ARBs and TTR. We interpreted this positive association as a mere reflection of a better control of blood pressure, as suggested in the ROCKET trial by the inverse association between systolic blood pressure and TTR.

Figure 1  Potential benefit of Mediterranean diet in the management of atrial fibrillation patients.
The study has clinical implications, as it shows that Med-Diet does not interfere with anticoagulation and could represent a dietary option for AF on VKAs. The suggestion to follow the Med-Diet may also be of useful some evidence to indicate that such a diet is associated with a lower risk of developing diabetes and metabolic syndrome, and with a reduction in stroke and MI risk (Figure 1). In accordance with this, adherence to Med-Diet was associated with lower risk of CVEs and neutral effect on bleeding.

Limitations

Adherence to Med-Diet was assessed by a short semi-quantitative questionnaire that not fully estimates the exact amount of each single food and, in particular, the consumption of leafy green vegetables, which have the highest content of vitamin K. An interventional study with a Med-Diet would be useful to further support the results of the present study.

Our suggestion to follow a Med-Diet is limited to AF patients on VKAs and the results stem from a single-centre study, therefore, a multicentre study needs to be done to support our conclusion.

Finally, the effect of Med-Diet should be explored also in AF treated with non-vitamin K oral anticoagulants to see if it is associated with a similar beneficial effect on cardiovascular risk.

Conclusion

In conclusion, adherence Med-Diet is not associated with changes in TTR in a cohort of AF patients suggesting that food contained in such diet does not interfere with VKAs.

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Conflict of interest: none declared.

References