

REFERENCE

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Are Omega-3 Fatty Acids Ineffective for Preventing Atrial Fibrillation Recurrence?

We read with great interest the paper by Macchia et al. (1). The FORWARD (Randomized Trial to Assess Efficacy of PUFA for the Maintenance of Sinus Rhythm in Persistent Atrial Fibrillation) trial involving 586 participants with symptomatic atrial fibrillation (AF) who already recovered normal sinus rhythm before being included in the study. There was no significant difference between the patients randomized to placebo or to omega-3 fatty acids for symptomatic recurrence of AF. The authors concluded that supplementation with 1 g of omega-3 fatty acids for 1 year did not reduce recurrent AF.

Are omega-3 fatty acids really ineffective for the prevention of atrial fibrillation recurrence? A meta-analysis indicated that in patients (3 studies and 485 patients) administered omega-3 fatty acids at least 4 weeks before cardioversion and continued thereafter, the recurrence rate of AF was obviously low (2). Metcalf et al. (3) demonstrated omega-3 fatty acids incorporated into human atrial cell membrane and reached a peak at about 30 days of treatment. Though omega-3 fatty acids can be increased in plasma and atrial tissue in short-term application, the concentration may be insufficient to develop the best antiarrhythmic effect (4). However, the patients in the FORWARD study were given omega-3 fatty acids started after cardioversion. So, maybe the duration of application before cardioversion is vital for its role.

Therefore, on the basis of current evidence we still can not reach a definite conclusion whether omega-3 fatty acids is effective for AF recurrence. Future large-scale, high-quality studies with patients being given omega-3 fatty acids at least 4 weeks prior to cardioversion are needed to verify our speculation and give a comprehensive evaluation of omega-3 fatty acids.

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Reply

We appreciate the letter of Dr. Guo and colleagues in which they raised doubts about if we can be definitive in closing the debate regarding the lack of efficacy of polyunsaturated fatty acids (n-3 PUFA) for the prevention of atrial fibrillation (AF). The authors raised an important and legitimate concern mentioning that omega-3 fatty acids may require time to be effectively incorporated into human cell membrane. Small systematic reviews seem to confirm this fact (1).

However, we still think that oral supplementation with n-3 PUFA is ineffective for at least 2 reasons. First, our updated and large systematic review that included 1,990 patients and 894 events (2) failed—in a meta-regression analysis—to find any association between supplementation and AF relapse, and disproved any relationship among dose amount, time of loading, or use of other antiarrhythmic therapies. Second, patients in the FORWARD (Randomized Trial to Assess Efficacy of PUFA for the Maintenance of Sinus Rhythm in Persistent Atrial Fibrillation) trial (3) who received more than 30 days of “loading dose” of n-3 PUFA (those who did not have a recurrence within the first month of follow-up) presented the same rate of AF recurrence than those who did not receive omega-3.

In any case, we cannot affirm that a large and “definitive” clinical trial should not be conducted. However, we think that—in the context of secondary prevention of AF—we do have now strong evidence suggesting that oral supplementation should not be initiated to prevent AF relapse. On the other hand, this hypothesis is still untested in the setting of primary prevention of AF. In this context, large clinical trials may be conducted.

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