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Systematic Review/Meta-analysis

Efficacy and Safety of Omega-3 Fatty Acids for the Prevention of Atrial Fibrillation: A Meta-analysis

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ABSTRACT

Background: The effects of omega-3 fatty acids (PUFA) on the prevention of atrial fibrillation (AF) appear to contrast between several randomized controlled trials (RCTs). Therefore, we performed a meta-analysis to assess the efficacy and safety of PUFA for the primary and secondary prevention of AF.

Methods: PubMed, EMBASE, Web of Science, Cochrane Library and the Chinese Biomedical Literature Database were searched for randomized controlled trials (published up to January 2012) that compared PUFA with control. All statistical analyses were performed with RevMan (version 5.1; The Cochrane Collaboration, Oxford, United Kingdom).

Results: For primary prevention after open heart surgery: 6 studies with 928 patients were designed to evaluate the effects of PUFA on the incidence of postoperative AF. The use of PUFA significantly reduced the incidence of postoperative AF (odds ratio [OR] 0.66; 95% confidence interval [CI], 0.49 to 0.88; $P = 0.004$); there was no difference in complications or adverse events (OR, 1.24; 95% CI, 0.58-2.62; $P = 0.58$). For secondary prevention, we analyzed 5 studies involving 1256 patients designed to evaluate the effects of PUFA therapy on AF. The

RÉSUMÉ

Introduction : Plusieurs essais cliniques aléatoires (ECA) semblent s'opposer sur les effets des acides gras oméga-3 (AGPI) dans la prévention de la fibrillation auriculaire (FA). Cependant, nous avons réalisé une méta-analyse pour évaluer l'efficacité et l'innocuité des AGPI dans la prévention primaire et secondaire de la FA.

Méthodes : PubMed, EMBASE, Web of Science, la Bibliothèque Cochrane et la base de données sur la documentation biomédicale chinoise ont été examinés pour trouver des essais cliniques aléatoires (publiés jusqu'en janvier 2012) ayant comparé le groupe prenant des AGPI au groupe témoin. Toutes les analyses statistiques ont été réalisées à l'aide du RevMan (version 5.1; Collaboration Cochrane, Oxford, Royaume-Uni).

Résultats : Dans la prévention primaire après une chirurgie à cœur ouvert, 6 études incluant 928 patients ont été élaborées pour évaluer les effets des AGPI sur l'incidence de la FA postopératoire. L'utilisation des AGPI a réduit de façon significative l'incidence de la FA postopératoire (ratio d'incidence approché [RIA] 0,66; intervalle de confiance [IC] de 95 %, 0,49 à 0,88; $P = 0,004$); il n'y a eu aucune différence dans les complications ou les événements indésirables (RIA, 1,24; IC

Atrial fibrillation (AF) is a very common disease. It is estimated that the prevalence of AF is 0.4%-1% in the general population and prevalence increases with age.[1,2] AF is also the most common sustained cardiac rhythm disturbance in clinical practice, accounting for approximately one-third of hospitalizations for arrhythmia.[3] AF is closely associated with an increased long-term risk of stroke,[4] congestive heart failure, all-cause mortality,[5] and decreased quality of life. However, no current therapy (drug, device, or ablation) is entirely optimal in terms of efficacy, and several available therapies may be harmful.[3,6,7] Thus, safer pharmacological agents are being sought.

The upstream therapy, which includes angiotensin-converting enzyme inhibitors, aldosterone receptor antagonists, statins, glucocorticoids, and omega-3 fatty acids (PUFA), may deter the development of new AF or, when established, decrease its rate of recurrence or progression to permanent AF.[8] PUFA, which is mainly present in oily fish has received more and more attention in the medical and scientific literature in recent years. It mainly contains eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). PUFA is believed to possess anti-inflammatory properties, antiarrhythmic effects, antifibrotic effects, and most importantly, appears to be well tolerated.[9-13] However, evidence for the effects of PUFA on the

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use of PUFA did not significantly reduce the recurrence of AF (OR, 0.74; 95% CI, 0.39-1.42; $P = 0.37$); no difference was observed in complications or adverse events (OR, 1.10; 95% CI, 0.78-1.57; $P = 0.58$).
Conclusions: The meta-analysis shows that PUFA therapy is significantly associated with a decreased odds of incidence of AF after open heart surgery, but there is no significant difference in recurrence of AF between PUFA and control groups. PUFA is well-tolerated, with no difference in complications or adverse events between PUFA and control groups.

de 95 %, 0,58-2,62; $P = 0,58$). Dans la prévention secondaire, nous avons analysé 5 études incluant 1256 patients pour évaluer les effets du traitement par AGPI sur la FA. L'utilisation des AGPI n'a pas réduit de façon significative la récurrence de la FA (RIA, 0,74; IC de 95 %, 0,39-1,42; $P = 0,37$); aucune différence n'a été observée dans les complications ou les événements indésirables (RIA, 1,10; IC de 95 %, 0,78-1,57; $P = 0,58$).
Conclusions : La méta-analyse montre que le traitement par AGPI est associé de façon significative à une diminution de l'incidence de la FA après la chirurgie à cœur ouvert, mais il n'y a aucune différence dans la récurrence de la FA entre le groupe prenant des AGPI et le groupe témoin. Les AGPI sont bien tolérés, et aucune différence n'a été observée dans les complications ou les événements indésirables entre le groupe prenant des AGPI et le groupe témoin.

prevention of AF seems to be conflicted. PUFA has shown significant antiarrhythmic effects in rat atrial myocytes.[14] A prospective cohort study[15] has shown that consumption of baked or broiled fish 1-4 times per week for 12 years was associated with a 31% lower risk of developing AF compared with fish consumption of less than once a week. However, 3 population-based studies[16-18] provided conflicting findings. Moreover, a number of randomized controlled trials (RCTs) have examined the effects of PUFA on the prevention of AF over the past decade. These studies have also generated contrasting results due to the limited sample sizes and different inferences from the individual studies. Therefore, we performed a meta-analysis of RCTs to assess the efficacy and safety of using PUFA in the primary (new-onset AF after open heart surgery) and secondary (recurrence of AF) prevention of AF.

Methods

Study selection

All studies (up to January 11, 2012) evaluating the efficacy and/or safety of PUFA for the prevention of AF were initially searched from 5 electronic search engines—PubMed, EMBASE, Web of Science, Cochrane Library, and the Chinese Biomedical Literature Database—by 2 independent investigators (Z.H. and L.Y.). The search terms included "atrial fibrillation," "omega-3 fatty acids," "eicosapentaenoic acid," "docosahexaenoic acid," and "fish oils." Moreover, we manually searched references from selected studies and recent review articles. Finally, we used search engine Google Scholar to obtain more related articles. No language restriction was imposed. We also contacted relevant authors and pharmaceutical companies to obtain complete information.

The reviewers (Z.H. and L.Y.) independently selected the studies to be included in the analysis and resolved disagreements by discussion or consensus of a third reviewer (J.T.). A study was included in the meta-analysis if it met all of the following specified criteria: (1) RCT; (2) patients of at least 18 years old scheduled for open heart surgery or electrical cardioversion, or with symptomatic persistent/paroxysmal AF; (3) comparing PUFA with control; and (4) reporting any of the following outcomes: incidence of postoperative AF (POAF) (POAF is defined as an episode of AF that lasted >5 minutes, or clinically recognized AF), recurrence of AF, complications, and adverse events.

Data extraction and quality assessment

The 2 reviewers (Z.H. and L.Y.) independently performed data extraction using a data extraction form prepared for the analysis. Disagreements were resolved by discussion or involving a third reviewer (J.T.). The following information was extracted from each study: (1) study methods and designs: randomization, allocation concealment, blinding, and withdrawals/dropout; (2) baseline characteristics of patients: sex, age, body weight, and concomitant drug therapy; (3) baseline characteristics of included studies: inclusion and exclusion criteria, details of treatments, follow-up duration, and documentation of AF; and (4) study outcomes: incidence of POAF, recurrence of AF, complications, and adverse events.

The same reviewers independently assessed the methodological quality of every study using the Jadad scale.[19] Disagreements were resolved by discussion or involving a third reviewer (J.T.). Studies were scored according to the presence of 3 key methodological features of randomization (0-2 points), blinding (0-2 points), and withdrawals/dropout (0-1 point). The quality score ranged from 0 to 5 points. A score of 2 or less is considered a low-quality study and a score of at least 3 is considered a high-quality study.

Statistical analysis

We performed quantitative analysis of individual study data using standard statistical procedures provided in RevMan5.1 (The Cochrane Collaboration, Oxford, United Kingdom). The odds ratio (OR) for each study outcome was calculated to allow for pooling of similar outcomes. If statistical heterogeneity between studies was not observed, OR was calculated using a fixed effects model. If statistical heterogeneity was found, OR was calculated using a random effects model. Statistical heterogeneity was assessed using the χ^2 test and was quantified using the I^2 statistic. A P value less than or equal to 0.10 was considered statistically significant for heterogeneity.[20] An I^2 value of 0% indicates no observed heterogeneity, whereas a value >50% indicates substantial heterogeneity.[21] Sensitivity analysis was performed in a predefined manner to assess the effect of the following: (1) primary prevention: intravenous PUFA preparation; and (2) secondary prevention: the paroxysmal AF population; studies in which not all of the patients underwent electrical cardioversion therapy, low-quality studies (Jadad score ≤2). The possibility of publication bias was assessed by the funnel plot and Egger's test analysis. A two-tailed P value <0.05 was considered to be significant.

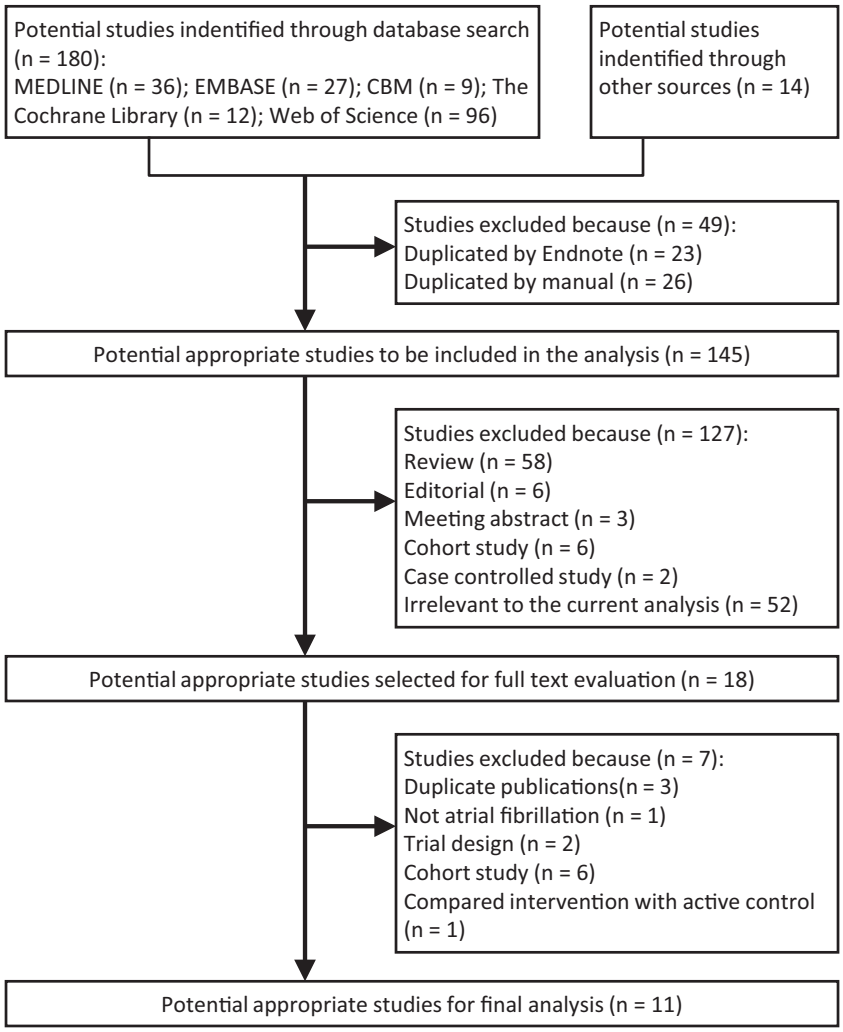

Figure 1. Selection process for randomized controlled trials on atrial fibrillation and omega-3 fatty acids (PUFA). CBM, Chinese Biomedical Literature Database.

Results

Identified studies

The selection process of the included RCTs is shown in Figure 1. We included a total of 11 RCTs[22-32] with 2184 patients that met our inclusion criteria. Six studies with 928 patients[22-27] investigated the primary prevention of PUFA in patients undergoing open heart surgery and 5 studies with 1256 patients[28-32] investigated the use of PUFA in patients with AF as secondary prevention. The baseline characteristics of the included studies and the assessment of study quality (Supplemental Table S1) are shown in Table 1.

Quantitative findings

Primary prevention after open heart surgery. Combination of the results of the 6 relevant studies[22-27] revealed that the incidence of POAF was significantly lower (29.4 vs 37.7%; $P = 0.007$; Table 2) in patients undergoing open heart surgery who received PUFA therapy compared with control. The overall OR for the 6 studies was 0.66 (95% confidence interval [CI], 0.49-0.88; $P = 0.004$; Fig. 2) in a fixed-effects model for PUFA-treated patients vs control-treated patients. No significant heterogeneity was observed between these studies ($P = 0.12$ and $I^2 = 44\%$; Fig. 2). We also used a random effects model to assess the effect of PUFA on the prevention of POAF considering that there was significant clinical heterogeneity between the studies, both in terms of results (some positive, some negative or neutral) and in terms of the PUFA formulations, dosage, and duration of therapy. The result (OR, 0.65; 95% CI, 0.44-0.96; $P = 0.03$; Supplemental Fig. S1) was similar to that using a fixed effects model. Then we conducted a sensitive analysis according to the previous section. After removing the study by Heidt et al.[24] which was a study of a single intravenous infusion of PUFA, the overall outcome remained the same (OR, 0.68; 95% CI, 0.50-0.92; $P = 0.01$; Table 3). There was no evidence of publication bias according to the funnel plot (Supplemental Fig. S2) and Egger's test analysis ($P = 0.79$).

Four studies[23,25-27] reported complications and adverse events. Statistical heterogeneity between the studies was present ($P = 0.06$ and $I^2 = 59\%$; Table 3), thus the random effects model was used. Pooled data from the 4 studies demonstrated no significant difference (43.7% vs 40.1%; $P = 0.361$; Table 2;

Table 1. The baseline characteristics of the included studies and the assessment of study quality

Study first author, year	Type of study	Study population	Intervention	N	Age	Male, %	Concomitant drug, %			Follow-up duration	Quality score
							BB	Statin	RASi		
Primary prevention after open heart surgery											
Calo, 2005[27]	R, OL	Post CABG, SR	Usual care plus 2 g per d PUFA (EPA: 0.57 g per d; DHA: 1.15 g per d)	160	65.5	86	57.5	56.9	79.4	Four wk after discharge	3
Heidt, 2009[24]	R, DB	Post CABG, SR	Fish oil 100 mg/kg body weight per d (EPA: 1.65 g per d; DHA: 1.83 g per d)	102	66.4	73	NR	NR	NR	Intensive care unit period	3
Heidarsdottir, 2010[26]	R, DB, P	Post open heart surgery, SR	Two soft capsules PUFA (EPA: 1.24 g per d; DHA: 1.00 g per d)	168	67.0	82	76.2	NR	NR	Until discharge or 2 wk after the surgery	4
Saravanan, 2010[25]	R, DB, P	Post CABG, SR	PUFA, 2 g per d (EPA: 0.94 g per d; DHA: 0.78 g per d)	104	66.0	77	85.4	98.1	73.5	Until discharge	5
Farquharson, 2011[23]	R, DB, P	Post open heart surgery	Fish oil 15 mL per d (EPA: 2.7 g per d; DHA: 1.9 g per d)	194	64.0	82	41.2	73.0	56.7	Six d or until discharge	5
Sorice, 2011[22]	R	Post CABG, SR	PUFA 2 g per d (EPA: 0.57 g per d; DHA: 1.15 g per d)	105	63.5	79	60.2	65.7	55.2	Until discharge	3
Secondary prevention											
Kowey, 2010[31]	R, DB, P	Symptomatic paroxysmal or persistent AF	PUFA 8 g per d loading dose for 7 d (EPA: 3.72 g per d; DHA: 3.00 g per d); PUFA maintenance dose 4 g per d (EPA: 1.86 g per d; DHA: 1.50 g per d)	663	60.5	60	70.0	45.0	39.0	Six mo	5
Bianconi, 2011[32]	R, DB, P	Persistent AF and post ECV	PUFA 3 g per d before (EPA: 1.39 g per d; DHA: 1.16 g per d); PUFA 2 g per d after ECV (EPA: 0.93 g per d; DHA: 0.77 g per d)	204	69.3	71	44.9	NR	66.8	Six mo	5
Ozaydin, 2011[30]	R, OL	Persistent AF and post ECV	PUFA 2 g per d (EPA: 0.36 g per d; DHA: 0.24 g per d) plus amiodarone	47	61.0	48	26.1	30.4	73.9	One y	2
Nodari, 2011[29]	R, DB, P	Persistent AF and post ECV	PUFA 2 g per d (EPA: 0.93-0.96 g per d; DHA: 0.77-0.80 g per d), amiodarone	199	69.5	70	61.8	48.7	100.0	One y	5
Kumar, 2012[28]	R, OL	Persistent AF and post ECV	Fish oil 6 g per d (EPA: 1.02 g per d; DHA: 0.72 g per d)	178	62.0	82	NR	38.2	55.1	360 d	2

AF, atrial fibrillation; BB, β-blocker; CABG, coronary artery bypass grafting; DB, double blind; DHA, docosahexaenoic acid; ECV, electrical cardioversion; EPA, eicosapentaenoic acid; NR, not reported; OL, open-label; P, placebo; PUFA, omega-3 fatty acids; R, randomized; RASi, renin-angiotensin system inhibitors; SR, sinus rhythm.

Table 2. Incidence of clinical outcomes

Outcomes	Sample size (n)	Treatment group, % (n)	Incidence, % (n)	*P* value, χ^2 test
Primary prevention after open heart surgery				
The incidence of postoperative atrial fibrillation	928	PUFA: 49.5 (459)	29.4 (135)	0.007
		Control: 50.5 (469)	37.7 (177)	
Complications and adverse events	625	PUFA: 49.8 (311)	43.7 (136)	0.361
		Control: 50.2 (314)	40.1 (126)	
Secondary prevention				
The recurrence of atrial fibrillation	1256	PUFA: 50.2 (631)	52.3 (330)	0.565
		Control: 49.8 (625)	53.9 (337)	
Complications and adverse events	928	PUFA: 50.6 (634)	12.2 (135)	0.575
		Control: 49.4 (620)	11.6 (177)	

PUFA, omega-3 fatty acids.

OR, 1.24; 95% CI, 0.58-2.62; $P = 0.58$) between PUFA and control groups.

Secondary prevention. Five studies,[28-32] totaling 1256 patients, evaluated the effects of PUFA use on the recurrence of AF. In analysis of the 5 studies, the recurrence of AF was not significantly lower (52.3% vs 53.9%; $P = 0.565$; Table 2) in PUFA-treated patients compared with control-treated patients. The overall OR for the 6 studies was 0.74 (95% CI, 0.39-1.42; $P = 0.37$; Fig. 3) in a random-effects model. There was significant heterogeneity ($P = 0.0001$; $I^2 = 83\%$).

To find the origin of the heterogeneity we subsequently performed sensitivity analyses according to the previous section. When we excluded the paroxysmal AF populations in the study by Kowey et al.,[31] the overall OR was 0.79 (95% CI, 0.37-1.70; $P = 0.54$; Table 3). Results were similar when ORs were calculated after exclusion of the study by Kowey et al.[31] in which not all patients underwent electrical cardioversion therapy (OR, 0.62; 95% CI, 0.27-1.40; $P = 0.25$, Table 3). When we limited the study to high quality studies (Jadad score ≥3), the overall OR was 0.95 (95% CI, 0.49-1.81; $P = 0.87$; Table 3). There was no evidence of publication bias by Egger's test analysis ($P = 0.40$), whereas the examination of the funnel plot revealed asymmetry (Supplemental Fig. S3).

Four studies[28,29,31,32] reported complications and adverse events. Statistical heterogeneity among the studies was not present ($P = 0.19$ and $I^2 = 36\%$; Table 3), thus the fixed effects model was used. Pooled data from the 4 studies demonstrated no significant difference (12.2% vs 11.6%; $P = 0.575$; Table 2; OR, 1.10; 95% CI, 0.78-1.57; $P = 0.58$) between PUFA and control groups.

Discussion

Our meta-analysis shows that PUFA therapy was associated with a 34% decreased odds of AF after open heart surgery compared with control. A nonsignificant 26% reduced odds of recurrence AF was observed in patients treated with PUFA in comparison with control-treated patients. There is no significant difference in both primary prevention after open heart surgery and secondary prevention between PUFA and control groups in complications and adverse events. These results add some clarity in the area that has been very uncertain, as reflected in the Canadian Cardiovascular Society guidelines.[33]

Primary prevention after open heart surgery

PUFA significantly reduced the incidence of AF after open heart surgery. The mechanisms of the preventive effect of PUFA on POAF have been in part delineated. A possible role of inflammation in the pathophysiology of POAF has been repeatedly suggested,[9,34] and the anti-inflammatory activity of PUFA is now well-documented.[10,12] This might explain a potential preventive effect of PUFA on AF. The study by Sorice et al.[22] showed that PUFA administration significantly reduced the incidence of POAF in patients undergoing coronary artery bypass graft (CABG) surgery, and the benefit of PUFA therapy seemed more marked in patients undergoing on-pump CABG. This finding may further support the hypothesis of an anti-

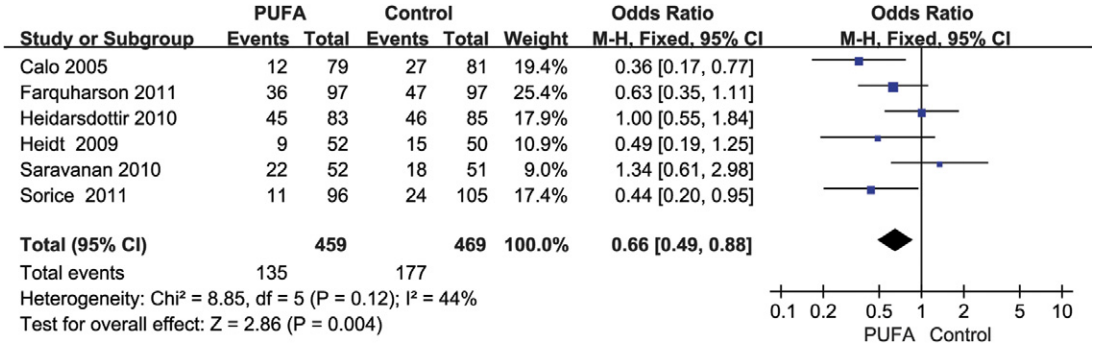

Figure 2. Effect of omega-3 fatty acids (PUFA) vs control on the incidence of postoperative atrial fibrillation. CI, confidence interval; df, degree of freedom; M-H, Mantel-Haenszel.

Table 3. Sensitivity analyses and the safety of PUFA

	N*	Events/total		OR (95% CI)	*P* value	Heterogeneity		Analysis model
		PUFA	Control			χ^2 *P* value	I^2	
Primary prevention after open heart surgery								
Removing 1 study with intravenous PUFA preparation	5[22,23,25-27]	126/407	162/419	0.68 (0.50-0.92)	0.01	0.08	52%	RE
Complications and adverse events	4[23,25-27]	136/311	126/314	1.24 (0.58-2.62)	0.58	0.06	59%	RE
Secondary prevention								
Recurrence of AF in persistent AF patients	5[28-32]	195/373	208/356	0.79 (0.37-1.70)	0.54	0.0002	82%	RE
Recurrence of AF after ECV	5[28-30,32]	163/309	190/302	0.62 (0.27-1.40)	0.25	0.002	80%	RE
Removing Jadad score ≤ 2 studies	3[29,31,32]	260/517	250/514	0.95 (0.49-1.81)	0.87	0.004	82%	RE
Complications and adverse events	4[28,29,31,32]	77/634	69/620	1.10 (0.78-1.57)	0.58	0.19	36%	FE

AF, atrial fibrillation; CI, confidence interval; ECV, electrical cardioversion; FE, fixed effects model; OR, odds ratio; PUFA, omega-3 fatty acids; RE, random effects model.

*N indicates number of remaining studies.

inflammatory PUFA action considering that on-pump CABG induces a systemic inflammatory response by triggering the production and release of inflammatory mediators.

Several studies also documented the efficacy of PUFA administration in preventing POAF. A prospective cohort study[15] showed that consumption of baked or broiled fish 1 to 4 times per week for 12 years was associated with a 31% lower risk of developing AF compared with fish consumption less than once a week. In another observational study,[35] high DHA had a protective effect on AF in men during an average follow-up of 17 years. An open-label prospective RCT[27] reported a significant reduction ($P = 0.013$) in the incidence of AF after CABG surgery in patients who received a supplement of approximately 1.7-1.8 g of EPA and DHA for a minimum of 5 days before CABG and continued until discharge. In another study,[24] investigators used high concentrations of n-3 PUFA (100 mg/kg body weight per day) as an intravenous infusion for a short period (24-72 hours) in the perioperative phase and observed similar benefits.

In contrast with our results, Liu et al.[36] and Benedetto et al.[37] reported that PUFA had no significant effects on the prevention of POAF. There are some differences between the present meta-analysis and the previous ones. First, primary prevention is totally different from secondary prevention. Primary prevention is defined as the prevention of disease or mental disorders in susceptible individuals or populations using specific practices, whereas secondary prevention is defined as the prevention of recurrences or exacerbations of a disease that has already been diagnosed. Unfortunately, primary prevention and secondary prevention were not separated at the beginning in the study by Liu et al.[36] Second, approximately half of the studies included in the meta-analysis by Liu et al. were published in abstract form. These studies which were not submitted for peer review may influence the results, heterogeneity, and publication bias. Finally, the study by Benedetto et al.[37] only included 3 RCTs and did not have large enough sample sizes.

Secondary prevention

Our meta-analysis showed that there was no significant difference between PUFA and control groups in recurrence of AF. Very recently, one large RCT[31] also reported that the use of a high dose of PUFA (4 g per day, content of DHA 1.50 g per day) did not reduce recurrent AF in patients with paroxysmal or persistent AF. However, there are several experimental studies[14,38,39] and an epidemiological study[15] supporting an atrial antiarrhythmic recurrence effect of PUFA. There are several plausible explanations for these controversial results.

First, experimental studies were conducted in animal hearts which have a significantly smaller remodelling capacity compared with diseased human hearts. Furthermore, the dose used in clinical trials is generally lower than that applied in animal experiments and could be insufficient to achieve a direct effect on ion channels.

Second, as mentioned above, the total daily dose of PUFA and the percentage levels of DHA in the PUFA may influence

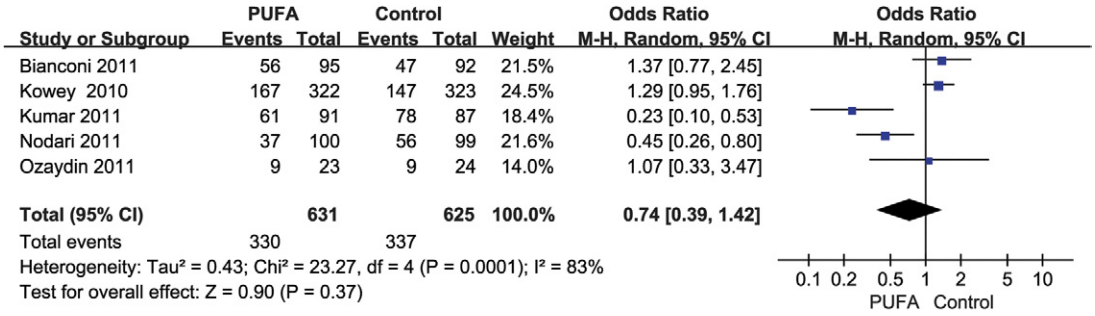

Figure 3. Effect of omega-3 fatty acids (PUFA) vs control on the recurrence of atrial fibrillation. CI, confidence interval; df, degree of freedom; M-H, Mantel-Haenszel.

the efficacy of PUFA on the prevention of AF. In the secondary prevention studies, serum DHA levels increased to a lesser extent than EPA levels: in the study by Kowey et al.,[31] median percent change from baseline in EPA was more than 230%, whereas DHA levels only changed by 100%; Bianconi et al.[32] also reported that EPA levels more than doubled, whereas DHA levels only increased by 25%.

Moreover, the period of administration was too short before electrical cardioversion. An interesting study[40] showed that incorporation of PUFA into human atrial cell membrane phospholipids continued to increase over time after achieving stable plasma concentrations, suggesting the possibility of delayed antiarrhythmic effect of PUFA. It also showed that the maximum membrane PUFA content was observed at about 1 month of treatment at the dose of 6 g per day, and most recurrences of AF after direct-current cardioversion occurred within the first month.[3] Participants who received a loading dose of PUFA may have increased the blood concentrations of PUFA. However, participants received only a 7-day loading dose of PUFA in the study by Kowey et al. and Bianconi et al. This progressive increase in PUFA content in phospholipids may explain the early lack of efficacy in secondary prevention trials.[41] Therefore, it may be a plausible explanation that the period of administration before electrical cardioversion was too short to allow a sufficient incorporation of PUFA into atrial membranes.

Study limitations

There are several problems which need to be taken into consideration for valid interpretation of the observed PUFA effects. First, consumption of fish products with a high PUFA content was associated with a decrease in the occurrence of AF,[15] but dietary information on participants' fish consumption during and before trials was not collected in most included studies. Second, there were significant differences in concomitant drug therapy which may have confounded results as they themselves reduce the incidence of POAF[42,43] and result in different response to PUFA therapy. Finally, the total daily dose of PUFA and ratio of EPA to DHA were highly variable in the included studies, and the 2 components may have different effects.[35] Therefore, the optimal regimen remains unknown.

Conclusions

Our meta-analysis demonstrates modest benefits from PUFA in primary prevention of POAF, supporting the concept that PUFA supplementation is safe and can be administered as an emerging treatment option to all patients undergoing open heart surgery. Although some authors have stated that the agent is of limited value, and its ultimate role in preventing new-onset AF in other clinical conditions remains untested, the agent may still have value as an adjunctive therapy. In secondary prevention, although no significant difference is found between PUFA and control groups, there is still a 26% odds reduction in AF recurrence. Therefore, more studies are needed to further confirm our findings and to determine whether treatment with PUFA may prevent new-onset AF in other clinical conditions and prevent AF recurrence.

Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at http://dx.doi.org/10.1016/j.cjca.2012.03.019.