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Omega-3 polyunsaturated fatty acids in the prevention of postoperative atrial fibrillation in open heart surgery: a systematic review and meta-analysis

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Aim. To evaluate the literature data on the efficacy of omega-3 polyunsaturated fatty acids (PUFAs) in the prevention of postoperative atrial fibrillation (POAF) in elective cardiac surgery, including on- or off-pump coronary artery bypass grafting and/or valve replacement and/or repair.
Material and methods. The search for studies was carried out using the PubMed database and Google Scholar from 2005 to January 31, 2022. From the initially identified search results, 19 articles were analyzed. The design of articles corresponded to randomized clinical trials. Omega-3 PUFAs was selected as an interventional effect. The studies were to include, as an end point, the assessment of new POAF cases in the early period after open heart surgery.
Results. The meta-analysis included 15 studies with 3980 patients, of which 1992 (50,0%) patients took omega-3 PUFAs. POAF occurred in 587 (29,5%) patients receiving omega-3 PUFAs and 679 (34,2%) patients on standard therapy (hazard ratio, 0,8, 0,68-0,93, p=0,004). There is a variation in effect size for POAF patients in the presented randomized clinical trials relative to the axis of the central trend and heterogeneity of studies with a significant number of patients included (I^2=51%, p=0,01).
Conclusion. Our systematic review and meta-analysis showed the effectiveness of omega-3 PUFAs in the prevention of POAF during open heart surgery.

Keywords: omega-3 polyunsaturated fatty acids, atrial fibrillation, cardiac surgery.

Relationships and Activities: none.

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Omega-3 polyunsaturated fatty acids (PUFAs), primarily eicosapentaenoic (EPA) and docosahexaenoic acids (DHA), decrease the risk of cardiovascular events by reducing the incidence of supraventricular and ventricular arrhythmias [1]. Analysis of the cellular and molecular mechanisms of omega-3 PUFA action is relevant for the prevention of arrhythmias.

The use of omega-3 PUFAs to prevent new episodes of atrial fibrillation (AF) in the early postoperative period of open-heart surgery is controversial. The first studies demonstrated the effectiveness of prescribing omega-3 PUFAs in the short-term perioperative period of coronary artery bypass grafting (CABG) [2, 3]. More recent studies have shown opposite results, showing that omega-3 PUFAs do not lead to an additional reduction in the risk of postoperative AF (POAF) [4, 5]. Thus, conflicting data on the antiarrhythmic effect of omega-3 PUFAs in patients undergoing cardiac surgery in terms of the prevention of POAF raises questions. Systematic review and meta-analysis will determine the effectiveness of omega-3 PUFAs in the short term to prevent new cases of AF in cardiac surgery.

The aim of this review was to evaluate literature data on the efficacy of omega-3 PUFAs in the prevention of POAF during elective cardiac surgery, including on- or off-pump CABG and/or heart valve repair/replacement.

Material and methods

Search for publications and selection of studies. The search for information was carried out in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) [8] in the PubMed and Google Scholar database and included research search using search queries, keywords (including MeSH) and logical operators. Poster presentations, dissertations, symposiums, case reports, books, meta-analyses, systematic reviews, review articles, letters to readers, recommendations, animal studies were not used according to the search goal. English and Russian were established as the main language of literature.

Keywords in the PubMed database: (omega-3 polyunsaturated fatty acids) AND (postoperative atrial fibrillation) AND (coronary artery bypass graft) AND (cardiac surgery). To search the Google Scholar database, we used the query: omega-3 polyunsaturated fatty acids AND postoperative atrial fibrillation AND coronary artery bypass graft AND cardiac surgery.

The PICO (population, intervention, comparator, outcome) model was used to search for studies. The last search was carried out on January 31, 2022. The systematic review included randomized controlled trials (RCTs) where the initial data were adequately presented — study design, clinical characteristics of patients, type of intervention, control and comparison group. Cardiac surgical interventions such as on- and off-pump CABG, and/or heart valve repair/replacement were taken into account. Omega-3 PUFAs, prescribed in the perioperative period for the prevention of POAF, was chosen as an interventional effect. The studies were to include as an endpoint an assessment of POAF risk by electrocardiographic monitoring or recording.

Risk of bias. The risk of bias for individual studies included in the systematic review was assessed using The Cochrane Collaboration's tool for assessing risk of bias. The overall risk of bias was assessed in 6 domains: random sequence generation; allocation concealment; blinding of patients and personnel; blinding of outcome assessment; incomplete outcome data and selective reporting [12, 13].

Statistical analysis. Statistical processing was performed using Review Manager (RevMan), version 5.4.1 (The Cochrane Collaboration, 2020). The meta-analysis was carried out according to the random effects model, using the inverse dispersion method. The results of meta-analysis were presented as a forest plot. Statistical heterogeneity was assessed using Pearson's chi-square test and heterogeneity index ($I^2>40\%$, $p<0,10$). Meta-analysis of the absolute values in the study and control groups was performed according to the data on absolute values, taking into account the number of subjects in the compared groups. We assessed the efficacy of omega-3 PUFAs in addition to standard therapy compared with standard therapy using odds ratios (OR) with 95% confidence intervals (CI).

Results

Data extraction and synthesis. Primary screening using the search queries described above yielded 23 PubMed publications and 924 results using the Google Scholar database. Of the 947 results found, 44 posts were duplicated, so only non-duplicate search results were left.

The study did not include symposiums, case reports and case series, books, meta-analyzes, systematic reviews, reviews, letters to readers, guidelines, animal studies. After analyzing the titles and their abstracts, 122 publications contained full-text articles. Evaluation of full-text copies resulted in the exclusion of 102 publications due to lack of specified data or submission of sub-analysis. Thus, the initially identified search results, the summary quantitative data of 19 articles (2,0%) were processed using statistical analysis (Figure 1). Subsequently, a detailed analysis of each article was carried out with an assessment of the study design, which allowed the selection of RCTs. English and Russian have been set as the language limit.

The analysis of each presented study took into account information on the number of patients in each group, type of cardiac surgery, blinding, incidence of POAF, placebo, duration of omega-3 PUFA therapy, methods for verifying POAF, and follow-up duration.

Characteristics of the included RCTs. The main characteristics of RCTs meeting the inclusion criteria are presented in Table 1.

Assessement of bias risks. The risks of bias in the included RCTs were assessed in accordance with the Cochrane Collaboration questionnaire (Tables 2, 3). It should be noted that most RCTs were open-label. This could affect performance and detection bias. Ten studies did not note the results of randomization sequence generation, while concealment of the randomization sequence was not specified in 11 studies, and was absent in 3 studies (selection bias). Two studies did not specify, and 1 study did not specify outcome biases (attrition bias). Sixteen studies were not specified and 2 studies lacked information on the presentation of study results (selective reporting).

An evaluation of the included RCTs showed that 4 studies, due to the high risk of bias, could not be used for meta-analysis, as a result of which they were excluded [18-21]. For the remaining studies, design, methodology, and patient characteristics were con-

Table 1

Characteristics of the included studies

Author, year	Type of surgery	Blinding	N (treatment/ control)	Control group	Dose of omega-3 PUFAs	Duration of administration	Criteria for AF	Duration of monitoring	Duration of follow-up
Calo, 2005 [2]	Off-pump CABG (n=19 (23,7%) patients), on-pump	Open-label	160 (79/81)	Standard therapy	Omega-3 PUFA 2 g/day (EPA:DHA = 1:2)	24-36 hours after surgery and until discharge	AF >5 min or requiring intervention	Continuous ECG monitoring for 4-5 days, then daily ECG recording until discharge	4 weeks after discharge
Heidt, 2009 [3]	On-pump CABG	Double-blind	102 (52/50)	Soybean oil 100 mg/kg per day	Fish oil 100 mg/kg per day (EPA:DHA = 0,9:1)	Continuous infusion started before surgery and continued until transfer to the ICU	AF >15 min	Continuous ECG monitoring in the ICU, then daily ECG	Until discharge
Saravanan, 2010 [4]	On-pump CABG	Double-blind	103 (52/51)	Olive oil 2 g/day	Omega-3 PUFAs 2 g/ day (EPA:DHA = 1,2:1)	At least 5 days before surgery and continued until discharge	AF ⩾30 sec	Continuous ECG monitoring for 5 days, then daily ECG recording	During inpatient treatment
Heidarsdottir, 2010 [6]	Off-pump CABG (n=20 (11,9%) patients), on-pump CABG (n=103 (61,3%) patients), heart valve repair/replacement (n=45 (26,8%) patients)	Double-blind	168 (83/85)	Olive oil 2 g/day	EPA 1,24 g/ day, DHA 1 g/ day.	5-7 days before surgery and until discharge or 2 weeks after surgery	AF >5 min	Continuous ECG monitoring in the ICU	During inpatient treatment (<14 days)
Sorice, 2011 [7]	Off-pump CABG (n=93 (46,3%) patients), on-pump CABG (n=108 (53,7%) patients)	Not indicated	201 (96/105)	Standard therapy	Omega-3 PUFAs 2 g/ day (EPA:DHA = 1:2)	5 days before surgery and until discharge	AF >5 min or requiring intervention due to hemodynamic instability	Continuous ECG monitoring for 4 days after surgery, and then daily ECG recording or in case of complaints	In the hospital
Farquharson, 2011 [8]	On-pump CABG (n=122 (62,9%) patients), combination of CABG and heart valve repair/ replacement (n=72 (37,1%) patients)	Double-blind	194 (97/97)	Sunflower oil 15 ml/ day	Omega-3 PUFAs 15 ml/ day (2,7 g EPA and 1,9 g DPC)	3 weeks before surgery	AF >10 min or requiring intervention	Continuous ECG monitoring for 72 hours, then daily ECG recording	In the hospital

Table 1. Continuation

Author, year	Type of surgery	Blinding	N (treatment/control)	Control group	Dose of omega-3 PUFAs	Duration of administration	Criteria for AF	Duration of monitoring	Duration of follow-up
Sandesara, 2012 [9]	Off-pump CABG (n=61 (25,1%) patients), on-pump CABG (n=154 (63,4%) patients), combination of CABG and heart valve replacement (n=28 (11,5%) patients)	Double-blind	243 (120/123)	Corn oil 2 g/day	Omega-3 PUFAs 4 g/day (EPA:DHA = 1,24:1)	Up to 16 days	AF or atrial flutter requiring intervention	Continuous ECG monitoring and ECG recording	14 days
Mozaffarian, 2012 [10]	Off-pump CABG (n=460 (30,3%) patients), valve replacement (n=785 (51,8%) patients), radiofrequency ablation (12 (0,8%) patients). Not specified (259 (17,1%) patients)	Double-blind	1516 (758/758)	Olive oil 2 g/day	Omega-3 PUFAs 1 g/day (EPA:DHA = 1,24:1)	3-5 days before surgery and at least 10 days after surgery	AF ⩾30 sec	Continuous ECG monitoring for 5 days and daily ECG recording or when arrhythmia occurs	In the hospital
Veljović, 2013 [11]	On-pump CABG	Not indicated	40 (20/20)	Standard therapy	Omega-3 PUFAs 100 ml	4 days before surgery 100 ml omega-3 PUFAs at a rate of 25 ml/h	AF >5 min	ECG recording every 6 hours for the first 24 hours for 48 hours	In the hospital
Stanger, 2014 [12]	On-pump CABG (n=24 (61,5%) patients), CABG and valve replacement (n=15 (20,0%) patients)	Double-blind	39 (19/20)	Standard therapy	Omega-3 PUFAs 0,5 ml/kg/body weight before surgery, 50 ml after surgery	3 infusions (42 hours and 18 hours before surgery and 42 hours after surgery)	According to ECG	ECG recording every day	3 days
Wilbring, 2014 [13]	On-pump CABG	Not indicated	198 (99/99)	Standard therapy	Omega-3 PUFAs 2 g/day (EPA:DHA = 1,24:1)	5 days before surgery and until discharge	According to ECG	Continuous ECG monitoring until discharge	In the hospital
Lomivorotov, 2014 [14]	On-pump CABG	Double-blind	39 (18/21)	Standard therapy	Omega-3 PUFAs 200 mg/kg/day	200 mg/kg/day, within 24 hours before induction of anesthesia followed by 100 mg/kg/day after surgery from days 2 to 7	AF >30 sec within 10 days after surgery	Continuous ECG monitoring	2 years

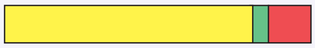
Table 1. Continuation

Author, year	Type of surgery	Blinding	N (treatment/ control)	Control group	Dose of omega-3 PUFAs	Duration of administration	Criteria for AF	Duration of monitoring	Duration of follow-up
Feguri, 2017 [15]	On-pump CABG	Double-blind	28 (14/14)	Standard therapy	Omega-3 PUFA 0,2 mcg/kg	4-hour intraoperative infusion	ECG recording	ECG recording	In the hospital
Joss, 2017 [16]	On-pump CABG (n=373 (66,7%) patients), CABG and/ or valve replacement (n=186 (33,3%) patients)	Double-blind	561 (284/275)	Mineral oil 2 g/day	Omega-3 PUFAs 2 g/ day (EPA:DHA = 3:2)	5 days before surgery and after surgery for 4 weeks	AF >5 min or requiring intervention due to hemodynamic instability	Telemonitoring or ECG recording	Within 4 weeks after surgery
Farahani, 2017 [17]	Off-pump CABG (n=29 (7,2%) patients), on-pump CABG (n=372 (92,8%) patients)	Double-blind	401 (202/199)	Olive oil 2 g/ day	Omega-3 PUFAs 2 g/day (EPA:DHA = 1,5:12)	5 days before surgery and until discharge	AF >5 min	Continuous ECG monitoring until discharge	In the hospital
Belan, 2014 [18]	On-pump CABG	Open-label	120 (60/60)	Standard therapy	Omega-3 PUFAs 2 g/day (EPA:DHA = 1,2:1)	5 days before surgery and after surgery for 3 months	ECG recording	Continuous ECG monitoring in the ICU, then daily ECG recording until discharge and in case of complaints	In the hospital
Kolesnikov, 2015 [19]	On-pump CABG	Open-label	73 (33/40)	Standard therapy	Intravenous infusion of omega-3 PUFA emulsion at a dose of 100 ml per day	Once in the first 5-7 days after the operation	AF >30 sec within 7-10 days after surgery	ECG recording	In the hospital
Panov, 2008 [20]	CABG (not specified)	Open-label	189 (94/95)	Standard therapy	Omega-3 PUFA at a dose of 2 g/day	7±4 days before CABG, and early after surgery (24-36 h) and continued for 14 days	ECG recording	Continuous ECG monitoring in the ICU, then daily ECG recording until discharge and in case of complaints	In the hospital
Rubanenko, 2017 [21]	On- and off-pump CABG	Open-label	102 (51/51)	Standard therapy	Omega-3 PUFAs before surgery at a dose of 2 g/day and at a dose of 1 g/day after operation	On average, 5 days before surgery and within 3 weeks after operation	ECG recording	Continuous ECG monitoring in the ICU, then daily ECG recording until discharge	In the hospital

Abbreviations: DHA — docosahexaenoic acid, CABG — coronary artery bypass grafting, ICU — intensive care unit, PUFAs — polyunsaturated fatty acids, AF — atrial fibrillation, ECG — electrocardiogram, EPA — eicosapentaenoic acid.

Table 2

**Assessment of the risks of bias in the included RCTs.
The authors' judgments about each element of the risk of bias in percent
for all included RCTs are presented**

Random sequence generation	Selection bias	
Allocation concealment	Selection bias	
Blinding of patients and personnel	Performance bias	
Blinding of outcome assessment	Detection bias	
Incomplete outcome data	Attrition bias	
Selective reporting	Reporting bias	

■ — low risk ■ — uncertain risk ■ — high risk

Table 3

Summary assessment of the bias risk. An overview of the authors' judgments about each element of the bias risk for each included RCT is presented

	Random sequence generation	Allocation concealment	Blinding of patients and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting
Calo, 2005	+	?	−	?	+	?
Heidt, 2009	?	?	+	?	+	?
Saravanan, 2010	+	?	+	+	+	?
Heidarsdottir, 2010	?	?	+	?	+	?
Sorice, 2011	?	?	?	?	+	+
Farquharson, 2011	+	+	+	+	+	?
Sandesara, 2012	?	?	+	+	+	?
Mozaffarian, 2012	+	+	+	?	+	?
Veljović, 2013	?	?	?	?	?	?
Stanger, 2014	+	?	+	?	+	−
Wilbring, 2014	?	?	?	?	+	?
Lomivorotov, 2014	+	+	+	?	−	−
Feguri, 2017	+	?	+	+	+	?
Joss, 2017	+	+	+	?	+	?
Farahani, 2017	+	+	+	?	?	?
Panov, 2008	?	−	−	−	+	?
Belan, 2014	?	−	−	−	+	?
Kolesnikov, 2015	?	−	−	−	+	?
Rubanenko, 2017	?	?	−	−	+	?

■ — low risk ■ — uncertain risk ■ — high risk

sistent with the aim of this study. The results of the meta-analysis are presented in Figure 2.

Assessment of the risk of publication bias. Figure 3 shows a funnel plot. Noteworthy is the scatter in the size of effects for patients with POAF in the presented RCTs relative to central tendency axis. Some asymmetry of the funnel plot is noted with a considerable number of studies included in the analysis.

Ultimately, the meta-analysis included 15 studies with 3980 patients, of which 1992 (50,0%) patients were taking omega-3 PUFAs. POAF occurred in 587 patients on omega-3 PUFAs and 679 patients on standard therapy (hazard ratio, 0,8, 0,68-0,93, p=0,004; I^2=51%, p=0,01).

Discussion

Data from our systematic review and meta-analysis demonstrated a favorable effect of omega-3 PUFAs in the prevention of POAF during open heart surgery. Our results are consistent with previous information from the literature [22]. An important difference of our systematic review is the inclusion of Russian papers [18-21]. On the other hand, domestic publications on the study of omega-3 PUFA effect on the prevention of POAF showed a high risk of bias, which was the reason for not including these sources in the meta-analysis.

The effectiveness of the use of omega-3 PUFAs is due to the anti-inflammatory, antioxidant effect, which determines the incidence of this arrhythmia [20, 21]. It was shown that patients with POAF during surgery had higher malondialdehyde levels in the atrial tissues compared with patients without arrhythmia (4,47 µmol/mg vs 3,85 µmol/mg protein, p<0,01). There was a strong direct correlation both in the placebo and treatment group between the level of malondialdehyde in atrial tissues and in the blood. Among patients receiving omega-3 PUFAs, the concentration of C-reactive protein was 35,4% less, while leukocytosis was 32,5% higher compared with the control group. This study demonstrated that a strategy of prescribing omega-3 PUFAs with vitamins C and E not only reduced the occurrence of arrhythmia, but also reduced the oxidative stress. This short-term, safe treatment has improved the outcomes of patients undergoing on-pump cardiac surgery [23].

Wang H, et al. (2018), Wilbring M, et al. (2014) on the effectiveness of omega-3 PUFAs in the prevention of POAF is inconsistent with the data of Gu J, et al. (2016), Stanger O, et al. (2014) [12, 13, 22, 24]. For example, elevated serum and atrial concentrations of omega-3 PUFAs, EPA, or DHA have not been associated with a reduction in AF [25] or inflammation [26] in some studies.

Domestic publications also demonstrate the favorable effect of omega-3 PUFAs in reducing the risk of POAF, which, according to our results, leads to a decrease in the severity of hemodynamic disorders and the length of stay in the hospital [18-21]. In addition, a study by Rubanenko OA, et al. (2017) showed that patients taking omega-3 PUFAs have a lower concentration of interleukin-6 in the postoperative period, as an inflammation factor, myeloperoxidase and superoxide dismutase, as markers of oxidative stress, which confirms the additional effects of the drug [21].

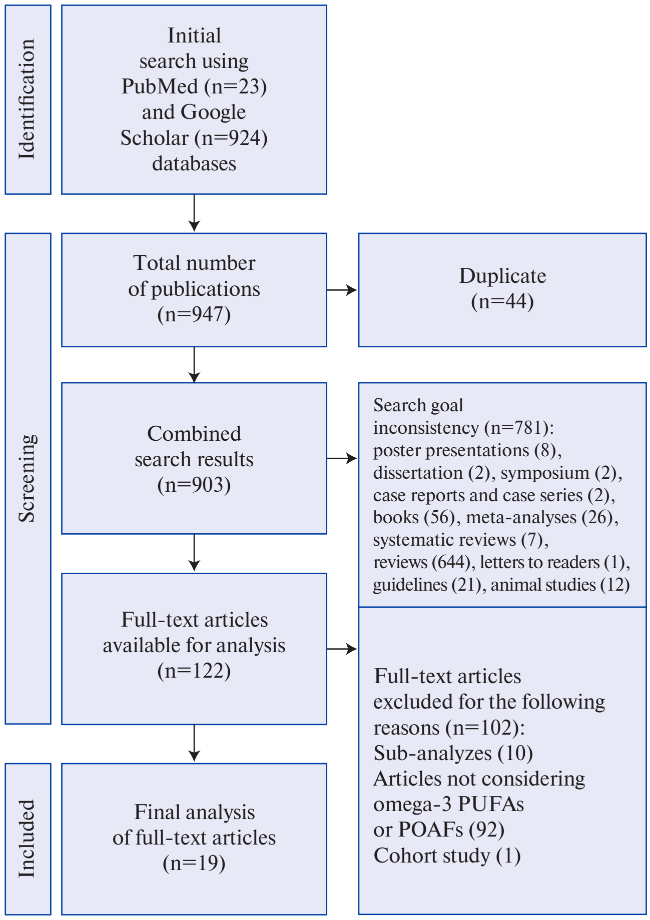


Figure 1. Publication selection algorithm.
Abbreviations: PUFAs — polyunsaturated fatty acids, POAF — postoperative atrial fibrillation.

Omega-3 index test can characterize the individual response to the drug and contribute to a better understanding of the pharmacokinetics and pharmacodynamics of PUFAs. Considering the results of the Garg PK, et al. (2021), showing a U-shaped relationship between the concentration of PUFAs and AF, the prevention of arrhythmia will depend on personal targeted incorporation of omega-3 acids into cell membranes [27].

In 2018, a meta-analysis was conducted, where out of 269 identified articles, 14 studies were included involving 3570 patients [28]. PUFAs reduced the incidence of POAF (OR, 0,84 (95% CI 0,73-0,98), p=0,03). Subgroup sensitivity analysis found that omega-3 PUFAs were effective in preventing POAF for an EPA/DHA ratio <1 (OR, 0,51 (95% CI 0,36-0,73), p=0,0003), but not in an EPA/DHA ratio >1 or an unknown ratio. In addition, efficacy in reducing POAF was evident when placebo was standard

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Feguri 2017	2	14	8	14	1.2%	0.25 [0.06, 0.97]
Calo 2005	12	79	27	71	4.8%	0.40 [0.22, 0.73]
Veljović 2013	4	20	8	20	2.0%	0.50 [0.18, 1.40]
Sorice 2011	11	96	24	105	4.2%	0.50 [0.26, 0.97]
Farahani 2017	17	201	29	199	5.2%	0.58 [0.33, 1.02]
Heidt 2009	17	52	27	50	6.7%	0.61 [0.38, 0.97]
Wilbring 2014	31	99	47	99	8.9%	0.66 [0.46, 0.94]
Stanger 2014	4	19	6	20	1.8%	0.70 [0.23, 2.10]
Farquharson 2011	36	97	47	97	9.6%	0.77 [0.55, 1.07]
Sandesara 2012	36	120	40	123	8.6%	0.92 [0.63, 1.34]
Mozaffarian 2012	227	758	233	758	14.7%	0.97 [0.84, 1.13]
Joss 2017	118	284	115	275	13.4%	0.99 [0.82, 1.21]
Heidarsdottir, 2010	45	83	46	85	11.0%	1.00 [0.76, 1.32]
Saravanan 2010	22	52	18	51	6.3%	1.20 [0.74, 1.95]
Lomivorotov 2014	5	18	4	21	1.6%	1.46 [0.46, 4.63]
Total (95% CI)		**1992**		**1988**	**100.0%**	**0.80 [0.68, 0.93]**
Total events	587		679			

Heterogeneity: Tau² = 0.04; Chi² = 28.35, df = 14 (P = 0.01); I² = 51%
Test for overall effect: Z = 2.89 (P = 0.004)

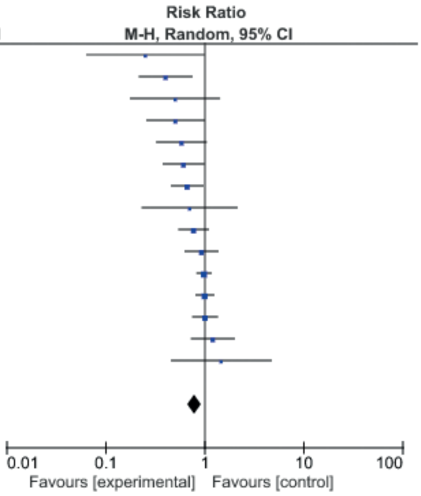


Figure 2. Random effects model comparing omega-3 PUFAs and standard therapy.
Note: the squares show the weighted effect size for each specific study (the square size corresponds to the weight of the studies); the bars show 95% CI; the diamond shows the weighted average of the POAF relative risk. Below in the experimental group is interpreted as a favorable sign.
Abbreviations: CI — confidence interval, POAF — postoperative atrial fibrillation.

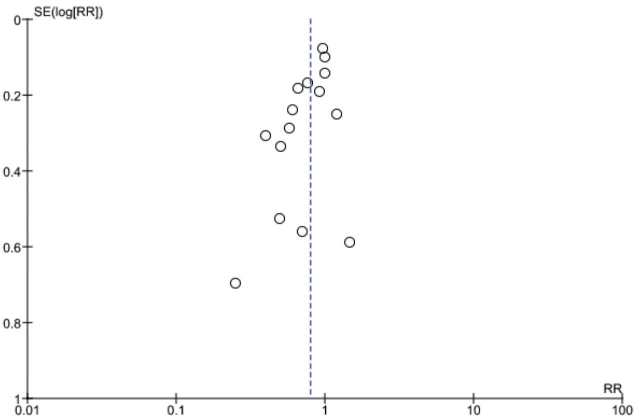


Figure 3. Risk of publication bias (funnel plot) of POAF prevention assessment with standard therapy and omega-3 PUFAs.
Note: vertical line represents the weighted average of the POAF risk ratio. This line reflects how much the experimental group is better (or worse) than the control group.
The funnel is formed because the accuracy of the effect estimate increases as the sample size increases. Therefore, smaller studies will form a wide bottom of the funnel (large variation in effect estimates cause small studies to be far from the weighted mean RR) and large studies will form a narrow top (greater accuracy in effect estimates, so that the results of such studies will not diverge far from weighted mean RR).
Abbreviations: POAF — postoperative atrial fibrillation, SE — standard error, RR — relative risk.

therapy versus placebo with fish oil inclusion (OR, 0,59 (95% CI 0,44-0,80), p=0,0005). Noteworthy that PUFAs reduced POAF after CABG (OR, 0,68 (95% CI 0,47-0,97), p=0,03), but not after other cardiac surgeries.

Thus, the results of our meta-analysis demonstrate the effectiveness of omega-3 PUFAs in reducing the risk of POAF during open heart surgery, including CABG and valvular replacement/repair. However, the analysis of Russian publications demonstrates the shortcomings in the collection and presentation of information on the subject of a systematic review, which may increase the risk of bias. Further prospects for omega-3 PUFA use dictate the need to determine the contingent of patients with coronary artery disease who are prescribed this drug in the perioperative period, mainly undergoing CABG, with an assessment of the omega-3 index as an indicator reflecting the content of omega-3 acids in the membrane of myocardial cells, factors of inflammation, oxidative stress, myocardial damage and dysfunction. This will make it possible to single out the group with the highest efficiency in prescribing omega-3 PUFAs.

Study limitations. This study has a number of limitations, many of which are related to design, in particular, the inclusion of patients undergoing off- or on-pump CABG and/or heart valve repair/replacement, the exclusion of cohort studies, and the presented heterogeneity of data from RCTs.

Conclusion

Our systematic review and meta-analysis showed the effectiveness of omega-3 PUFAs in patients with coronary artery disease in the prevention of POAF during off- or on-pump CABG and/or heart valve repair/replacement.

Relationships and Activities: none.

References

1. Tribulova N, Bacova BS, Benova TE, et al. Omega-3 Index and Anti-Arrhythmic Potential of Omega-3 PUFAs. Nutrients. 2017;9(11):1191. doi:10.3390/nu9111191.
2. Calò L, Bianconi L, Colivicchi F, et al. N-3 Fatty acids for the prevention of atrial fibrillation after coronary artery bypass surgery: a randomized, controlled trial. J Am Coll Cardiol. 2005;45(10):1723-8. doi:10.1016/j.jacc.2005.02.079.
3. Heidt MC, Vician M, Stracke SK, et al. Beneficial effects of intravenously administered N-3 fatty acids for the prevention of atrial fibrillation after coronary artery bypass surgery: a prospective randomized study. Thorac Cardiovasc Surg. 2009;57(5):276-80. doi:10.1055/s-0029-1185301.
4. Saravanan P, Bridgewater B, West AL, et al. Omega-3 fatty acid supplementation does not reduce risk of atrial fibrillation after coronary artery bypass surgery: a randomized, double-blind, placebo-controlled clinical trial. Circ Arrhythm Electrophysiol. 2010;3(1):46-53. doi:10.1161/CIRCEP.109.899633.
5. Mariscalco G, Sarzi Braga S, Banach M, et al. Preoperative n-3 polyunsatured fatty acids are associated with a decrease in the incidence of early atrial fibrillation following cardiac surgery. Angiology. 2010;61(7):643-50. doi:10.1177/0003319710370962.
6. Heidarsdottir R, Arnar DO, Skuladottir GV, et al. Does treatment with n-3 polyunsaturated fatty acids prevent atrial fibrillation after open heart surgery? Europace. 2010;12(3):356-63. doi:10.1093/europace/eup429.
7. Sorice M, Tritto FP, Sordelli C, et al. N-3 polyunsaturated fatty acids reduces post-operative atrial fibrillation incidence in patients undergoing "on-pump" coronary artery bypass graft surgery. Monaldi Arch Chest Dis. 2011;76(2):93-8. doi:10.4081/monaldi.2011.196.
8. Farquharson AL, Metcalf RG, Sanders P, et al. Effect of dietary fish oil on atrial fibrillation after cardiac surgery. Am J Cardiol. 2011;108(6):851-6. doi:10.1016/j.amjcard.2011.04.036.
9. Sandesara CM, Chung MK, Van Wagoner DR, et al. A Randomized, Placebo-Controlled Trial of Omega-3 Fatty Acids for Inhibition of Supraventricular Arrhythmias After Cardiac Surgery: The FISH Trial. J Am Heart Assoc. 2012;1(3):e000547. doi:10.1161/JAHA.111.000547.
10. Mozaffarian D, Marchioli R, Macchia A, et al. Fish oil and postoperative atrial fibrillation: the Omega-3 Fatty Acids for Prevention of Post-Operative Atrial Fibrillation (OPERA) randomized trial. JAMA. 2012;308:2001-11. doi:10.1001/jama.2012.28733.
11. Veljović M, Ristanović A, Popadić A, et al. Effects of preoperative administration of omega-3 PUFAs in the prevention of postoperative atrial fibrilation in myocardial revascularization. Serbian journal of anesthesia and intensive therapy. 2013;5(1-2):9-16.
12. Stanger O, Aigner I, Schimetta W, Wonisch W. Antioxidant supplementation attenuates oxidative stress in patients undergoing coronary artery bypass graft surgery. Tohoku J Exp Med. 2014;232(2):145-54. doi:10.1620/tjem.232.145.
13. Wilbring M, Ploetze K, Bormann S, et al. Omega-3 polyunsaturated Fatty acids reduce the incidence of postoperative atrial fibrillation in patients with history of prior myocardial infarction undergoing isolated coronary artery bypass grafting. Thorac Cardiovasc Surg. 2014;62(7):569-74. doi:10.1055/s-0034-1371699.
14. Lomivorotov VV, Efremov SM, Pokushalov EA, et al. Randomized trial of fish oil infusion to prevent atrial fibrillation after cardiac surgery: data from an implantable continuous cardiac monitor. J Cardiothorac Vasc Anesth. 2014;28(5):1278-84. doi:10.1053/j.jvca.2014.02.019.
15. Feguri GR, de Lima PRL, de Cerqueira Borges D, et al. Preoperative carbohydrate load and intraoperatively infused omega-3 polyunsaturated fatty acids positively impact nosocomial morbidity after coronary artery bypass grafting: a double-blind controlled randomized trial. Nutr J. 2017;16(1):24. doi:10.1186/s12937-017-0245-6.
16. Joss JD, Hernan J, Collier R, Cardenas A. Perioperative supplementation of polyunsaturated omega-3 fatty acid for the prevention of atrial fibrillation after cardiothoracic surgery. Am J Health Syst Pharm. 2017;74(1):e17-e23. doi:10.2146/ajhp150740.
17. Farahani AV, Azar AY, Goodarzynejad HR, et al. Fish oil supplementation for primary prevention of atrial fibrillation after coronary artery bypass graft surgery: A randomized clinical trial. Int J Surg. 2017;42:41-8. doi:10.1016/j.ijsu.2017.04.025.
18. Belan IA, Kizhvatova NV, Babicheva OV, et al. Omega-3 polyunsaturated fatty acids in the prevention of postoperative atrial fibrillation in patients undergoing aorto-coronary bypass surgery. Serdce: zhurnal dlya praktikuyushchih vrachej. 2014;79(5):324-8. (In Russ.)
19. Kolesnikov VN, Boeva OI, Yagoda AV, et al. Prevention of atrial fibrillation after direct myocardial revascularization: a randomized comparative study. Medical news of north caucasus. 2015;10(2):120-7. (In Russ.)
20. Panov AV, Tatarskiy BA, Gordeev ML, Nilk RI. Omega-3 polyunsaturated fatty acids in atrial fibrillation prevention after surgical myocardial revascularization. Rational Pharmacother. Card. 2008;3:26-30. (In Russ.)
21. Rubanenko OA, Fatenkov OV, Khokhlunov SM, et al. Combination of omega-3 polyunsaturated fatty acids and statins for the prevention of atrial fibrillation after coronary bypass surgery. Klin. med. 2017;95(9):817-23. (In Russ.) doi:10.18821/0023-2149-2017-95-8-693-699.
22. Wang H, Chen J, Zhao L. N-3 polyunsaturated fatty acids for prevention of postoperative atrial fibrillation: updated meta-analysis and systematic review. J Interv Card Electrophysiol. 2018;51(2):105-15. doi:10.1007/s10840-018-0315-5.
23. Rodrigo R, Prieto JC, Castillo R. Cardioprotection against ischaemia/reperfusion by vitamins C and E plus n-3 fatty acids: molecular mechanisms and potential clinical applications. Clin Sci (Lond). 2013;124(1):1-15. doi:10.1042/CS20110663.
24. Gu J, Lundbye-Christensen S, Eschen RB, et al. Marine n-3 fatty acids are incorporated into atrial tissue but do not correlate with postoperative atrial fibrillation in cardiac surgery. Vascul Pharmacol. 2016;87:70-5. doi:10.1016/j.vph.2016.11.004.
25. Dinesen PT, Schmidt EB. Marine n-3 fatty acids and the risk of new-onset postoperative atrial fibrillation after cardiac surgery. Vascul Pharmacol. 2016;87:23-5. doi:10.1016/j.vph.2016.11.005.
26. Joss JD, Hernan J, Collier R, Cardenas A. Perioperative supplementation of polyunsaturated omega-3 fatty acid for the prevention of atrial fibrillation after cardiothoracic surgery. Am J Health Syst Pharm. 2017;74(1):e17-e23. doi:10.2146/ajhp150740.
27. Garg PK, Guan W, Nomura S, et al. Plasma omega-3 and omega-6 PUFA Concentrations and Risk of Atrial Fibrillation: The Multi-Ethnic Study of Atherosclerosis. J Nutr. 2021;151(6):1479-86. doi:10.1093/jn/nxab016.
28. Wang H, Chen J, Zhao L. N-3 polyunsaturated fatty acids for prevention of postoperative atrial fibrillation: updated meta-analysis and systematic review. J Interv Card Electrophysiol. 2018;51(2):105-15. doi:10.1007/s10840-018-0315-5.