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"Perioperative administrations of omega three unsaturated fatty acids for reduction of postoperative atrial fibrillation in coronary artery bypass surgeries "

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ABSTRACT:

Introduction: Atrial fibrillation (AF) is frequently seen in the post-operative period following most cardiac surgeries. Despite advancements in surgical techniques and perioperative care, many patients after cardiac surgery remain susceptible for developing AF postoperatively specially patients undergoing coronary artery bypass surgery (CABG), and it may have an impact on the procedure's immediate and long-term results. Nevertheless, managing post-operative atrial fibrillation (POAF) presents numerous difficulties. In purpose of controlling and restricting the POAF, Polyunsaturated fatty acids (PUFA) have been administrated as a possible treatment option for POAF as they may have anti inflammatory effect and antiarrhythmic properties.

Methods: This is a prospective study which included two groups of all 100 ischemic heart disease patients who were scheduled for CABG. Group A consists of 50 patients who had preoperative omega three for 5 days and another 5 days post operative. Group B consists of 50 patients who didn't receive any omega-3. After up to five days of comparison, the outcomes between the two groups were noted.

Results: The incidence of POAF was low in group A than in group B and it was statistically significant over the first 5 days post operative. The two groups overall ICU stays were similar, while group A hospital stay was shorter overall, and was statistically significant.

Conclusions: According to the study findings, there is a lower incidence of postoperative atrial fibrillation in patients after CABG when they received perioperative omega-3 PUFA supplementation.

Keywords:
Post-operative Atrial fibrillation. Coronary artery bypass surgery. Omega three unsaturated fatty acid.

Background:

Cardiac surgery most commonly results in AF as a complication [1]. 11% to 40% of patients have this type of arrhythmia, more frequently following CABG [2, 4]. Even though AF is typically benign, self-limiting, and temporary, it can be linked to more serious complications, including heart failure, myocardial infarction, stroke, renal impairment, and neurological disorders. Reduced treatment, investigations, and total duration of admission are among the benefits of preventing POAF [5]. Following CABG, POAF typically manifests on postoperative days 2 to 5, with postoperative day 2 showing the highest prevalence [6, 7].

Recent studies have demonstrated that omega three polyunsaturated fatty acids, are more effective than other PUFA in reducing post operative A.F after CABG. It also demonstrated a reduction of the hospital stay period [5,8,9].

As PUFA boosts the non-arrhythmic duration in stage 4 respond and slightly hyperpolarizes the resting membrane potential of cardiomyocytes, it also exerts antiarrhythmic actions and improves the cell membrane stability, which provides significant protection against atrial fibrillation, and modulates the ion channels both directly and indirectly. [10-13].

During surgery, a hyperadrenergic condition is created, which results in elevated catecholamines and enhanced automatic activity. By lowering ventricular contractility, omega-3 PUFA lowers atrial fibrillation [14,15]. The anti-arrhythmic benefits could be related to omega-3 anti-inflammatory and anti-fibrotic properties, as well as modification of sympatho-vagal balance. [16].

In medical practice, omega-3 polyunsaturated fats are recently commonly employed. It has been demonstrated that PUFA therapy has cardioprotective effects and could reduce cardiac arrhythmias and sudden death in a variety of tests and studies [17]

Material and Methods:

This is a prospective single center study conducted between March 2020 and August 2023 at department of cardiothoracic surgery, Mansoura university hospital, Mansoura University, Egypt. This research was conducted on the patients who were scheduled for CABG. There were 100 patients in this research. The patients were classified into two groups: Group A, which consisted of 50 patients who received daily dose of 2 gm omega-3 PUFA divided into 2 doses starting 5 days before surgery till the 5th postoperative day, and Group B, which consisted of 50 patients who did not received omega-3. In both groups, the occurrence of atrial fibrillation during the perioperative phases was assessed.

Patients who had the following criteria were excluded: preoperative AF, patients having an ejection fraction of 40% or less, a history of myocardial infarction within 8 weeks, patients on anti-arrhythmic medication other than β-blockers, patients who had history of smoking or preoperative omega 3 intake in the last 3 months preoperative, and those receiving urgent, or redo CABG. Informed consent was obtained from each patient.

Perioperative preparation: A multidisciplinary team of cardiologists and cardiac surgeons thoroughly reviewed all patients prior to surgery. All patients were submitted to routine preoperative blood tests, physical examination, echocardiography, coronary angiography. Electrocardiogram (ECG) prior to surgery and Serum potassium (K) levels 7 days before surgery. Intraoperative monitoring for any recorded attacks of atrial fibrillation was done. The

assessment postoperatively included monitoring the patients by continuous ECG monitor in the ICU stay period and by 12 leads ECG twice per day at the ward through the first five postoperative days. Serum potassium was monitored daily starting from one day before surgery to the fifth postoperative day. All patients had serum k^+ level test and underwent 12 lead ECG upon discharge from the hospital and one month later. Attacks of AF were recorded if it lasted more than five minutes and was treated accordingly.

Statistical analysis and data interpretation:

Data was analyzed using SPSS (statistical package for social sciences) version 22. Qualitative data will be presented as number and percentage, Quantitative data will be tested for normality by Kolmogorov-Smirnov test then described as mean and standard deviation for normally distributed data and median and range for non-normally distributed. The appropriate statistical test was applied according to data type.

Results:

Age, gender, and BMI distributions of the 2 groups were homogeneous. Although mentioned, pre-existing risk factors for myocardial infarction, diabetes, heart failure, hypertension, and a history of obstructive pulmonary disease were not shown to be significant. The left atrium's diameter ranged between 34 and 44 mm, and the majority of patients have an ejection fraction of more than 45%. The difference was not statistically significant.(Table 1)

The obtained intra-operative data revealed no statistically significant differences regarding the number of grafts and duration of surgery in the 2 groups. However, intraoperative atrial fibrillation incidence was higher in group B than in group A, 8 (16%) patients in comparison to 2 (4%) patients, respectively. (Table 2)

The post-operative monitoring of the patients revealed less incidence of POAF in group A than group B over the first 5 days post operatively accompanied by a shorter hospital stay. The serum potassium level and ICU stay showed no significant difference in both groups. (Table 3)

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Table 1: Demographic data and the preoperative evaluation.

	Group A (n1=50) No. (%)	Group B (n2=50) No. (%)	P value	
			Chi square test	Student's t-test
Age (in years)				
41-50	1 (2.0)	1(2.0)		
51-60	8 (16.0)	15 (30.0)		
61-70	41 (82.0)	34 (68.0)		
Mean ±SD	64.14 ± 4.44	62.30 ± 5.29		0.063
Sex				
Male	40 (80.0)	41 (82.0)	0.790	
Female	10 (20.0)	9 (18.0)		
BMI (kg/m2)				
Underweight	1 (2.0)	1 (2.0)		
Normal	30 (60.0)	34 (68.0)		
Overweight	19 (38.0)	15 (30.0)		
Mean ±SD	24.17 ± 2.27	24.26 ± 2.16		0.845
Hypertension	32 (64.0)	34 (68.0)	0.658	
Diabetes mellitus	13 (26.0)	17 (34.0)	0.190	
Heart failure	3 (6.0)	4 (8.0)	(^{FE}p=1.000)	
History of myocardial infarction	32 (64.0)	31 (62.0)	0.461	
COPD	6 (12.0)	4 (8.0)	0.779	
Preoperative variables				
Serum Potassium (mmol/L)	4.11 ± 0.51	3.93 ± 0.47		0.068
LVEF (%)	58.9 ± 11.7	59.8 ± 11.1		0.674
Left atrial dimension (mm)	37.16 ± 3.82	38.36 ± 3.31		0.096
Number of diseased coronary vessels				
Single vessel	5 (10.0)	2 (4.0)	(^{FE}p=0.270)	
Double Vessel	12 (24.0)	18 (36.0)		
Triple Vessel	33 (66.0)	30 (60.0)		

BMI: **Body Mass Index**, COPD: **chronic obstructive pulmonary disease**, LVEF: **left ventricular ejection fraction ,** FE**: Fisher Exact**

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Table 2: Duration of surgery, number of grafts, and incidence of intraoperative AF.

	Group A (n1=50) No. (%)	Group B (n2=50) No. (%)	P value	
			Chi square test	Student's t-test
Duration of surgery (min)	295.3 ± 24.8	303.0 ± 29.9		0.164
Total number of grafts	2.38 ± 0.67	2.40 ± 0.57		0.872
Incidence of AF	2 (4.0 %)	8 (16.0%)	0.04*	

Table (3) Post-operative incidence of AF and serum potassium levels.

	Group A (n1=50) No. (%)	Group B (n2=50) No. (%)	P- value	
			chi- square test	students t-test
Incidence of POAF				
0 day	2 (4.0)	9 (18.0)	0.025*	
1st day	4 (8.0)	11 (22.0)	0.050*	
2nd day	4 (8.0)	16 (32.0)	0.003*	
3rd day	3 (6.0)	15 (30.0)	0.002*	
4th day	1 (2.0)	10 (20.0)	0.004*	
5th day	1 (2.0)	6 (12.0)	0.050*	
on discharge	2 (4.0)	5 (10.0)	^{FE}p=0.436	
1 month later	1 (2.0)	3 (6.0)	^{FE}p=0.617	
Serum Potassium level (mmol/L)				
0 day	4.08 ± 0.44	3.93 ± 0.46		0.100
1st day	4.05 ± 0.48	3.95 ± 0.41		0.244
2nd day	4.15 ± 0.46	3.98 ± 0.51		0.081
3rd day	3.97 ± 0.39	3.99 ± 0.50		0.827
4th day	3.94 ± 0.46	4.01 ± 0.45		0.470
5th day	4.11 ± 0.44	3.94 ± 0.48		0.072
On discharge	4.15 ± 0.46	4.11 ± 0.55		0.722
1 month later	4.08 ± 0.50	4.10 ± 0.48		0.775
ICU stay (days)	3.94 ± 0.46	4.01 ± 0.45		0.470
Post-operative hospital stay (days)	10.48 ± 1.07	12.04 ± 1.87		0.037*

FE**: Fisher Exact**

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Discussion:

The most prevalent arrhythmia arising after cardiac surgery is POAF in patients without a history of AF. The incidence of POAF ranges from 9.8-50%, and in the cohort research for Nikolaou and his colleagues, it was 28.5%. [19, 20].

Regarding the distribution of patient demographic characteristics (age, gender, and BMI), most of the patients were between the ages of 61 and 70, with groups A and B accounting for 41 (82.0%) and 34 (68.0%), respectively. Both groups had a higher proportion of male patients 40 (80.0%) and 41 (82.0%), respectively. Group A average BMI was 24.17 ± 2.27, whereas group B average was 24.26 ± 2.16. There is no statistically significant difference between both groups regarding age, gender, or BMI ($p = 0.063$, $p = 0.790$, and $p = 0.845$). Many studies have produced comparable findings [18, 19].

There was no statistically significant difference between both groups regarding risk factors and comorbidities. In Group A, 13 (26%) had Diabetes, 32 (64%) had hypertension, 32 (64%) had a history of acute coronary syndromes, 3 (6%) had heart failure and 6 (12%) had COPD, while in Group B, 17 (34%) had diabetes, 34 (68%) had hypertension, 31 (62%) had a history of acute coronary syndrome, 4 (8%) were in heart failure and 4 (8%) had COPD, and it was not statistically significant and was similar to the findings of the other studies [9,18].

Prior to surgery, both groups of patients were in sinus rhythm, according to the 12-lead electrocardiogram. Before surgery, serum potassium level was 4.1 ± 0.5 mmol/L in Groups A and 3.9 ± 0.4 mmol/L in Group B ($p = 0.068$). Most patients have three-vessel disease 33 (66.0%) in group A and 30 (60%) in group B, then two-vessel and one vessel disease. The difference was insignificant. Villareal and colleagues had comparable results [21].

Echocardiography revealed that Group A had a mean LVEF of 58.9% ± 11.7% and Group B had a mean LVEF of 59.8% ± 11.1% ($p = 0.674$). The left atrial diameter was 37.1 ± 3.8 mm in Group A and 38.3 ± 3.31 mm in Group B ($p = 0.096$). The difference is irrelevant and similar to the results of Calo and his colleagues [18]. The two groups had a mean LVEF of 55.3 ± 11.4% and 56.3 ± 12.1%, respectively, and left atrium diameters were 39.7 ± 5.2 mm and 38.36 ± 5.1 mm, respectively. The operation time in Group A was 295.3 ± 24.8 minutes, while in Group B it was 303.0 ± 29.9 minutes ($p = 0.164$). The difference was insignificant.

During the operation, 2 patients (4.0%) in group A and 8 patients (16.0%) in group B had AF ($p = 0.04$) which was statistically significant.

Post operatively, AF incidence in both groups was compared by continuous ECG analysis and 12 lead ECG from the zero to the fifth day post-operative. On the zero postoperative day, 2 patients (4.0%) in group A and 9 patients (18%) in group B ($p = 0.025$), in the first postoperative day, 4 patients (8.0%) versus 11 patients (22%) respectively ($p = 0.050$), the second postoperative day, 4 patients (8.0%) vs 16 patients (32%) respectively ($p = 0.003$), in the third postoperative day, 3 patients (6.0%) vs 15 patients (30%) respectively ($p = 0.002$), in the fourth postoperative day, 1 patients (2.0%) vs 10 patients (20%) respectively ($p = 0.004$), while in the fifth postoperative day, 1 patients (2.0%) vs 6 patients (12%) respectively ($p = 0.050$).

On discharge, a 12-lead ECG was utilized to compare the rates of atrial fibrillation between the two groups before discharge and one month later. On discharge, comparing group A and B revealed, 2 patients (4.0%) and 5 patients (10%), respectively ($p = 0.239$). 1 month after discharge, 1 patient versus 3 patients, (2.0%) to (6.0 %) respectively

(p = 0.307), which was not statistically significant. Maniscalco and colleagues discovered similar findings which revealed a statistically significant difference in the incidence of AF between both groups during hospital admission (p = 0.006) but not at discharge [22].

The mean ± standard deviation of serum potassium in both groups on similar days revealed no significant difference throughout the 1st five post-operative days (p = 0.081), (p = 0.827), (p = 0.470), (p = 0.072), (p = 0.072) respectively, on discharge (p = 0.722), and then after one month of hospital discharge (p = 0.775). In Group A, the average length of stay in the intensive care unit was 3.94 ± 0.46 day, while in Group B, it was 4.01 ± 0.45 and the mean difference showed no significance. Group A had a mean ± standard deviation of 10.4 ± 1 day and group B had 12 ± 2 days (p = 0.037). The average disparity is the most significant. Many other studies revealed similar results, with no statistically significant differences in duration of stay in intensive care in the two groups, although, there was significant differences in duration of hospital stay also [18, 22, 23].

In summary, group B had a higher incidence of POAF than group A during the surgery and for the first five days afterward, which was significant. Although the two groups' total stays in the intensive care unit were comparable, group A duration of stay was significantly shorter, with a significant mean difference.

The limitations of the study included a small sample size and only one month follow-up period. To guide clinical decisions and establish best practices for preventing postoperative arrhythmias in this setting, more extensive research with larger patient cohorts and controlled variables is still needed, even though our study demonstrated that Omega 3 PUFA shows effective role in preventing and controlling the incidence of POAF after coronary bypass surgery. More assessment and observation may also be suggested in longer-term research investigations.

Conclusion: The results of this study showed a correlation between perioperative administration of omega-3 PUFA supplementation and a decreased risk of new onset post operative AF. Over the course of the treatment, there was a decrease in the incidence of AF, which can have a significant effect on the result in terms of post-operative complications, duration of hospital stay, and quality of life. Accordingly, omega-3 polyunsaturated fatty acids may be utilized as a possible perioperative treatment for individuals undergoing CABG.

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References:

1. Costanzo S, Di Niro V, Di Castelnuovo A, Gianfagna F, Donati MB, De Gaetano G, Iacoviello L. Prevention of postoperative atrial fibrillation in open heart surgery patients by preoperative supplementation of n-3 polyunsaturated fatty acids: an updated meta-analysis. The Journal of thoracic and cardiovascular surgery. 2013 Oct 1;146(4):906-11. http://dx.doi.org/10.1016/j.jtcvs.2013.03.015

2. Habibollahi P, Jam SH, Vahdati SS, Baghi HM, Amiri H. Amiodaron in atrial fibrillation: post coronary artery bypass graft. World Journal of Emergency Medicine. 2016;7(4):250. http://dx.doi.org/10.5847/wjem.j.1920-8642.2016.04.002

3. Leitch JW, Thomson D, Baird DK, Harris PJ. The importance of age as a predictor of atrial fibrillation and flutter after coronary artery bypass grafting. The Journal of thoracic and cardiovascular surgery. 1990 Sep 1;100(3):338-42. http://dx.doi.org/10.1016/S0022-5223(19)35525-4

4. Creswell LL, Schuessler RB, Rosenbloom M, Cox JL. Hazards of postoperative atrial arrhythmias. The Annals of thoracic surgery. 1993 Sep 1;56(3):539-49. http://dx.doi.org/10.1016/0003-4975(93)90894-N

5. Zaman AG, Archbold RA, Helft G, Paul EA, Curzen NP, Mills PG. Atrial fibrillation after coronary artery bypass surgery: a model for preoperative risk stratification. Circulation. 2000 Mar 28;101(12):1403-8. http://dx.doi.org/10.1161/01.CIR.101.12.1403

6. Ommen SR, Odell JA, Stanton MS. Atrial arrhythmias after cardiothoracic surgery. New England Journal of Medicine. 1997 May 15;336(20):1429-34.. http://dx.doi.org/10.1056/NEJM199705153362006

7. Çağli K, Göl MK, Keles T, Şener E, Yildiz Ü, Uncu H, Taşdemir O, Bayazit K. Risk factors associated with development of atrial fibrillation early after coronary artery bypass grafting. American Journal of Cardiology. 2000 May 15;85(10):1259-61. http://dx.doi.org/10.1016/S0002-9149(00)00742-6

8. Heidt MC, Vician M, Stracke SK, Stadlbauer T, Grebe MT, Boening A, Vogt PR, Erdogan A. Beneficial effects of intravenously administered N-3 fatty acids for the prevention of atrial fibrillation after coronary artery bypass surgery: a prospective randomized study. The Thoracic and cardiovascular surgeon. 2009 Aug;57(05):276-80. http://dx.doi.org/10.1055/s-0029-1185301

9. Sorice M, Tritto FP, Sordelli C, Gregorio R, Piazza L. N-3 polyunsaturated fatty acids reduces post-operative atrial fibrillation incidence in patients undergoing â€ œon-pumpâ€ coronary artery bypass graft surgery. Monaldi Archives for Chest Disease. 2011;76(2). https://doi.org/10.4081/monaldi.2011.196

10. McLennan PL, Bridle TM, Abeywardena MY, Charnock JS. Dietary lipid modulation of ventricular fibrillation threshold in the marmoset monkey. American heart journal. 1992 Jun 1;123(6):1555-61. http://dx.doi.org/10.1016/0002-8703(92)90809-A

11. Kang JX, Leaf A. Prevention and termination of arrhythmias induced by lysophosphatidyl choline and acylcarnitine in neonatal rat cardiac myocytes by free omega-3 polyunsaturated fatty acids. Eur J Pharmacol. 1996;297:97-106.

12. Leaf A. The electrophysiological basis for the antiarrhythmic actions of polyunsaturated fatty acids. European heart journal supplements. 2001 Jun 1;3(suppl_D):D98-105. http://dx.doi.org/10.1016/S1520-765X(01)90127-0

13. Xiao YF, Wright SN, Wang GK, Morgan JP, Leaf A. Fatty acids suppress voltage-gated Na+ currents in HEK293t cells transfected with the α-subunit of the human cardiac Na+ channel. Proceedings of the National Academy of Sciences. 1998 Mar 3;95(5):2680-5. http://dx.doi.org/10.1073/pnas.95.5.2680

14. Hashimoto M, Shinozuka K, Gamoh S, Tanabe Y, Hossain MS, Kwon YM, Hata N, Misawa Y, Kunitomo M, Masumura S. The hypotensive effect of docosahexaenoic acid is associated with the enhanced release of ATP from the caudal artery of aged rats. The Journal of nutrition. 1999 Jan 1;129(1):70-6.http://dx.doi.org/10.1093/jn/129.1.70

15. Singer P. Blood pressure-lowering effect of mackerel diet. Klinische Wochenschrift. 1990 Jan 1;68:40-8.

16. Verma KK, Choudhary A, Kumar I. Pharmacological Potentials of Omega 3 Fatty Acid in Reduction of Atrial Fibrillation. Journal of Drug Delivery and Therapeutics. 2023 Mar 15;13(3):184-93. http://dx.doi.org/10.22270/jddt.v13i3.5766

17. Mozaffarian D, Psaty BM, Rimm EB, Lemaitre RN, Burke GL, Lyles MF, Lefkowitz D, Siscovick DS. Fish intake and risk of incident atrial fibrillation. Circulation. 2004 Jul 27;110(4):368-73. http://dx.doi.org/10.1161/01.CIR.0000138154.00779.A5

18. Calò L, Bianconi L, Colivicchi F, Lamberti F, Loricchio ML, de Ruvo E, Meo A, Pandozi C, Staibano M, Santini M. N-3 Fatty acids for the prevention of atrial fibrillation after coronary artery bypass surgery: a randomized, controlled trial. Journal of the American College of Cardiology. 2005 May 17;45(10):1723-8. http://dx.doi.org/10.1016/j.jacc.2005.02.0

19. Kaireviciute D, Aidietis A, Lip GY. Atrial fibrillation following cardiac surgery: clinical features and preventative strategies. European heart journal. 2009 Feb 1;30(4):410-25. http://dx.doi.org/10.1093/eurheartj/ehn609

20. Nikolaou M, Pattakos G, Hitas C, Koniari K, Pitsis A, Iliopoulos D, Xintarakou A, Vardas EP, Pattakos S, Tzeis S, Vardas P. ATRIAL FIBRILLATION POST CABG AND THE RISK OF ARRHYTHMIA RECURRENCE: THE AFRODITE STUDY. Hellenic Journal of Cardiology. 2024 Mar 5. http://dx.doi.org/10.1016/j.hjc.2024.03.003

21. Villareal RP, Hariharan R, Liu BC, Kar B, Lee VV, Elayda M, Lopez JA, Rasekh A, Wilson JM, Massumi A. Postoperative atrial fibrillation and mortality after coronary artery bypass surgery. Journal of the American College of Cardiology. 2004 Mar 3;43(5):742-8.http://dx.doi.org/10.1016/j.jacc.2003.11.023

22. Mariscalco G, Sarzi Braga S, Banach M, Borsani P, Bruno VD, Napoleone M, Vitale C, Piffaretti G, Pedretti RF, Sala A. Preoperative n-3 polyunsatured fatty acids are associated with a decrease in the incidence of early atrial fibrillation following cardiac surgery. Angiology. 2010 Oct;61(7):643-50. http://dx.doi.org/10.1177/0003319710370962

23. Langlois PL, Hardy G, Manzanares W. Omega-3 polyunsaturated fatty acids in cardiac surgery patients: An updated systematic review and meta-analysis. Clinical nutrition. 2017 Jun 1;36(3):737-46. http://dx.doi.org/10.1016/j.clnu.2016.05.013