

Effect of Omega-3 Polyunsaturated Fatty Acid on the Prevention of Atrial Fibrillation after Off-Pump Coronary Artery Bypass Grafting

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Abstract

Background: Postoperative atrial fibrillation (POAF) often occurs in patients after coronary artery bypass graft surgery (CABG), both conventional and off pump ranges from 11% to 40%. Although often transient, self-limited, and benign, it may be associated with increased postoperative morbidity. The prevention of POAF has been associated with improved postoperative outcomes in terms of reduced medical treatment, laboratory tests, shorter nursing time, and hospital stay, even when uncomplicated. The present study was conducted to find out the effect of omega polyunsaturated fatty acid on the prevention of POAF after off pump CABG.

Method: This cross-sectional study was conducted in the Department of Cardiac Surgery, National Institute of Cardiovascular Diseases (NICVD), Sher-E-Bangla Nagar, Dhaka, between September 2017 and August 2018. Total 100 patients with sinus rhythm admitted for OPCAB were included in this study, and they were divided into two groups, Group A, 50 patients having omega-3 PUFA in the preoperative and postoperative period up to the fifth postoperative day (POD) and Group B, 50 patients not having omega-3 PUFA in the preoperative and postoperative period up to the fifth POD. Findings were compared between two groups preoperatively, postoperatively, up to 5 days, at discharge, and at one month after discharge.

Results: Postoperative AF was significantly higher in group B in comparison to group A up to 5th POD. AF was present in a few patients during discharge and one month after discharge, but the differences were statistically not significant between groups. Total ICU stay was similar between the two groups, but the postoperative hospital stay was shorter in Group A, and the mean difference was statistically significant.

Conclusion: This study concluded that perioperative oral omega-3 polyunsaturated fatty acid intake reduces the incidence of postoperative atrial fibrillation in patients undergoing off pump coronary artery bypass graft surgery.

Key Words: Omega-3; Polyunsaturated fatty acid (PUFA); Postoperative Atrial fibrillation (POAF); Off-pump; Coronary artery bypass grafting (CABG).

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Introduction:

Post-Operative Atrial Fibrillation (POAF) is the most common complication that occurs in 25% after isolated coronary artery bypass grafting (CABG).¹⁻⁵ Although often transient, self-limited, and benign, atrial fibrillation (AF) may be associated with increased postoperative morbidity such as ventricular arrhythmias, myocardial infarction, heart failure, acute kidney injury, stroke, neurocognitive impairment, and infection.^{3,4}

The pathophysiological characteristics of POAF after cardiac surgery are multifactorial and has not yet been fully identified¹ and may be affected by preoperative factors like old age, hypertension, diabetes, obesity, heart failure, ischemic heart disease, chronic obstructive pulmonary disease (COPD); per-operative factors like surgical injury, atrial ischemia, pulmonary vein vent, acute volume changes; postoperative factors like volume overload, increased afterload and hypotension, β -blockers

withdrawal, right coronary artery occlusion, reduced left ventricular function and left ventricular hypertrophy are also risk factors as well.⁶ The main common pathway of all these is inflammation and oxidative stress.⁷⁻⁹ Surgical trauma to the atria is associated with an increased incidence of POAF, which explains why patients undergoing valvular surgery have the highest risk of developing POAF.^{1,10,11} Some studies suggest that less manipulation of the atria decreases atrial inflammation, and subsequently, AF.^{1,12} POAF after off-pump coronary artery bypass (OPCAB) most often develops between the 2nd to 5th postoperative day with a peak incidence in the 2nd and 3rd postoperative day.^{13,14}

The prevention of postoperative atrial fibrillation (POAF) has been associated with improved postoperative outcomes in terms of reduced medical treatment, laboratory tests, shorter nursing time, and hospital stay even when uncomplicated.¹⁵⁻²⁰ Considering that POAF is associated with a higher incidence of heart failure, stroke, prolonged hospital stay, and increased costs, it is justifiable to treat it.^{1,21}

Omega-3 polyunsaturated fatty acid (PUFA) has been widely used for clinical purposes. Clinical studies reported

that PUFA is effective in preventing POAF after CABG.²²⁻²⁴ PUFA therapy exerts a cardioprotective effect in different experimental and clinical reports, preventing cardiac arrhythmias and sudden death²⁵. Several studies have been shown that 2 gm (2 capsules) oral omega-3 PUFA supplementation at least five days prior to surgery up to the fifth postoperative day reduces the incidence of POAF and hospital stay significantly.^{22,24}

Omega-3 PUFA reduces AF by its anti-inflammatory effect²⁶⁻²⁹ and antiarrhythmic effect.³⁰⁻³⁴ It also reduces by reducing sympathetic outflow^{35,36}. It is also associated with reduced AF inducibility, maintenance, and structural remodeling of the heart by activating matrix metalloproteinase-9-mRNA expression and attenuating collagen turnover.³⁷ Despite its antiarrhythmic and anti-inflammatory characteristics, the use of this drug as a prophylactic agent against the occurrence of postoperative AF is uncommon, and yet the use of omega-3 PUFA as prophylaxis in patients undergoing OPCAB is not routine. The present study was conducted to investigate the effect of omega-3 PUFA in the reduction of post-OPCAB AF among Bangladeshi patients undergone off-pump CABG.

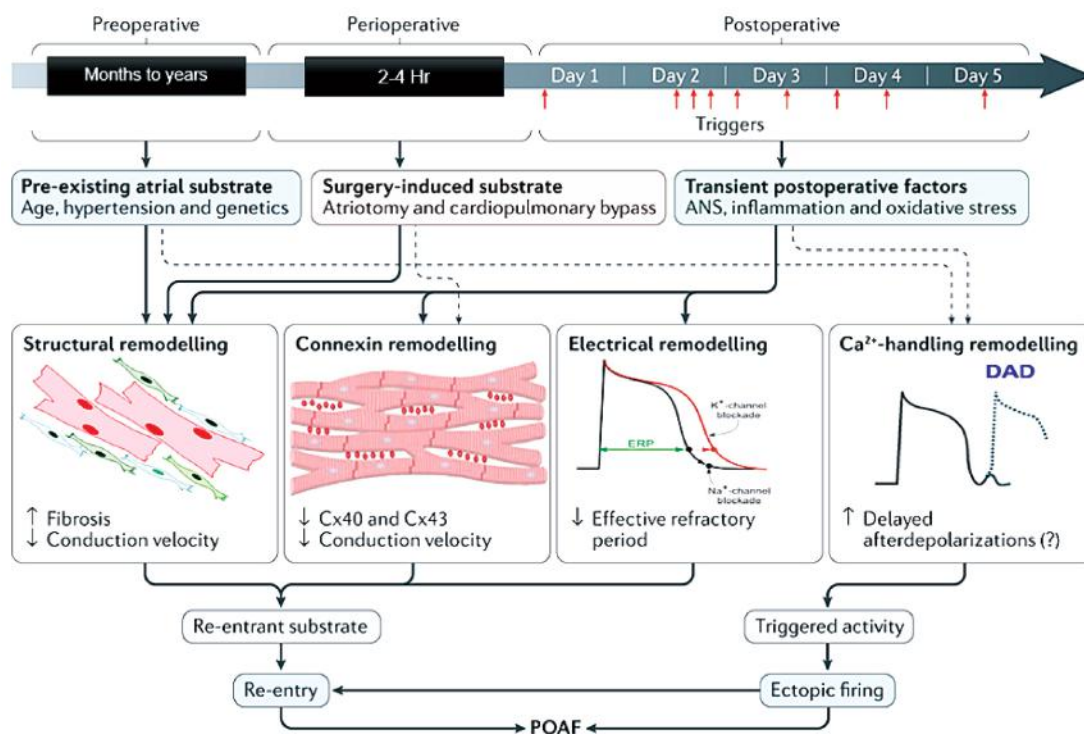


Fig.-1 : Mechanism of perioperative atrial fibrillation (POAF) and its interplay with surgery induced substrates

Methods and Materials

This cross-sectional study was conducted in the Department of Cardiac Surgery, National Institute of Cardiovascular Diseases (NICVD), Sher-E-Bangla Nagar, Dhaka, between the periods of 1st September 2017 and 31st August 2018. Purposively selected Patients who were admitted to the department of cardiac surgery at NICVD and planned for OPCAB. Patient with sinus rhythm admitted in the department of cardiac surgery at NICVD for OPCAB. Patients with a history of AF, patients with preoperative AF, patients with a history of MI within six weeks, patients on other antiarrhythmic drugs (Except β -blockers), left ventricular ejection fraction $d^{TM}35\%$, combined CABG and valve and other congenital heart surgery, conversion to on-pump CABG, redo CABG and urgent or emergency CABG were excluded from the study. Total 100 patients were included in the study, and they were divided into two groups, Group A, 50 patients with omega-3 PUFA in the preoperative and postoperative period up to 5th POD, and Group B, 50 patients without omega-3 PUFA in the preoperative and postoperative period up to 5th POD. Permission from the institutional review board and informed written consent from all patients were obtained for this study.

The patients were hospitalized at least seven days before surgery. Meticulous history was taken, and detailed clinical examinations were performed, and the presence of preoperative risk factors was recorded in predesigned structured proforma. Demographic data such as age, sex, BMI were recorded. Preoperative ECG, serum potassium using Dimension EXL with LM biochemistry analyzer, and echocardiogram were done in all patients under study. A 12-lead ECG was also done on the morning day of operation, just before the surgery. Omega-3 PUFA was prescribed at a dosage of one tablet (1 gm) twice times daily (2 gm/day) 5 days prior to surgery and up to 5th POD. Per operative occurrence of AF was assessed on OT monitor. After OPCAB surgery, each patient was transferred to the postoperative intensive care unit (ICU), and then on the 3rd postoperative day patient was transferred to a step-down or high dependency unit (HDU). In ICU and HDU, each patient was evaluated by continuous ECG monitor from the operative day, after arrival at ICU up to the fifth postoperative day. Serum potassium was measured daily from the operative day, after arrival at ICU, up to the fifth postoperative day. An episode of atrial fibrillation was counted if it persisted for more than five minutes and was treated accordingly. Total ICU stay and hospital stay after surgery were also recorded. A 12-lead ECG was done, and serum potassium was

measured for all patients on the day of hospital discharge and one month after discharge.

Results

The present study included 100 patients who were undergone OPCAB during the study period. Half of them were in Group A, preoperatively, and postoperatively on oral omega-3 PUFA, Group A and another half were in Group B, did not on oral omega-3 PUFA preoperatively and post operatively. Among the 50 patients of Group A, the highest number (78.0%) of patients were in the age group of 61-70 years followed by 51-60 years age group (20.0%), and the rest of them were in the 41-50 years age group (2.0%). Among the Group B patients, the highest number (60.0%) were in the age group of 61-70 years, followed by the age group of 51-60 years (38.0%), and the rest of them (2.0%) were in the age group of 41-50 years. Mean \pm SD of age among the patients of Group A and Group B was 64.14 \pm 4.44 and 62.30 \pm 5.29 years, respectively. Males were predominant in both groups, 82.0% patients in Group A and 84.0% patients in Group B. Mean(\pm SD) of BMI of the patients of Group A and Group B were 24.17 \pm 2.27 and 24.26 \pm 2.16, respectively. All the patients had some risk factors for coronary artery disease (CAD). In Group A, 70% were hypertensive, 24% were diabetic, 6% patients had heart failure, 82% patients had a history of MI, and 14% patients had COPD, and in Group B, 74% were hypertensive, 36% were diabetic, 4% patients had heart failure, 76% patients had history of MI and 16% patients had COPD (Table I).

Preoperative 12-lead ECG showed in all patients both the group, seven days prior to surgery and before the operation was in sinus rhythm. The mean \pm SD of serum potassium were 4.11 \pm 0.51 mEq/L and 3.93 \pm 0.47 mEq/L in Group A and Group B, respectively. The mean \pm SD of LVEF were 58.9 \pm 11.7% and 59.8 \pm 11.1% in Group A and Group B, respectively. The mean left atria anteroposterior dimensions were 37.16 \pm 3.82 mm and 38.36 \pm 3.31mm in Group A and Group B, respectively. In Group A, 10.0% patients had single coronary vessel disease, 24.0% patients had double coronary vessel disease, and 66.0% patients had triple vessel disease, and in Group B, 4.0% patients had single-vessel disease, 36.0% patients had double vessel disease, and 60.0% patients had triple vessel disease (Table II).

Mean \pm SD of the number of grafts were 2.38 \pm 0.67 in Group A and 2.40 \pm 0.57 in Group B, respectively. The mean \pm SD of operative time in Group A and Group B were 295.3 \pm 24.8 minutes and 303.0 \pm 29.9 minutes,

respectively. Regarding the occurrence of AF (OT monitor) per operatively, AF occurred in 4.0% of patients of Group A and 16% of patients of Group B (Table 2). On an operative day, after arrival at ICU, the mean±SD of serum potassium was 4.08±0.44 mEq/L and 3.93±0.46 mmol/L in Group A and Group B, respectively. On 1st POD, the mean±SD of serum potassium was 4.05±0.48 mmol/L and 3.95±0.41 mmol/L in Group A and Group B, respectively. On 2nd POD, the mean±SD of serum potassium were 4.15±0.46 mmol/L and 3.98±0.51 mmol/L in Group A and Group B, respectively. On 3rd POD, the mean±SD of serum potassium was 3.97±0.39 mmol/L and 3.99±0.50 mmol/L in Group A and Group B, respectively. On 4th POD, the mean±SD of serum potassium was 3.94±0.46 mmol/L and 4.01±0.45 mmol/L in Group A and Group B, respectively. On 5th POD, the mean±SD of serum potassium was 4.11±0.44 mmol/L and 3.94±0.48 mmol/L in Group A and Group B, respectively. At discharge, the mean±SD of serum potassium was 4.15±0.46 mmol/L and 4.11±0.55 mmol/L in Group A and Group B, respectively. After one month of discharge, the mean±SD of serum potassium was 4.08±0.50 mmol/L and 4.11±0.55 mmol/L in Group A and Group B, respectively.

On an operative day, after arrival at ICU, AF was present in 4.0% of patients and 18.0% patients in Group A and Group B, respectively. On 1st POD, AF was present in 8.0% of patients and 22.0% patients in Group A and Group B, respectively. On 2nd POD, AF was present in 8.0% of patients and 32.0% patients in Group A and Group B, respectively. On 3rd POD, AF was present in 6.0% of patients and 30.0% patients in Group A and Group B, respectively. On 4th POD, AF was present in 2.0% of patients and 20.0% of patients in Group A and Group B, respectively. On 5th POD, AF was present in 2.0% of patients and 12.0% patients in Group A and Group B, respectively (Figure-2). AF was present in 4.0% of patients and 10.0% patients in Group A and Group B, respectively, on the day of discharge. AF was present in 2.0% of patients and 6.0% of patients in Group A and Group B, respectively, after one month of discharge (Table 3). The mean±SD duration of ICU stay between Group A and Group B were 5.76±1.0 days and 5.46±0.65 days, respectively. The mean±SD of the duration of postoperative hospital stay in Group A and Group B was 10.48±1.07 days and 12.04±1.87 days, respectively (Table 2).

Table-I
Distribution of sociodemographic and comorbidities characteristics of the respondents

Variables	Groups		P-value
	Group A	Group B	
Age group f (%)			
41-50	01(02.0)	01(02.0)	
51-60	10(20.0)	19(38.0)	
61-70	39(78.0)	30(60.0)	
Mean(±SD)	64.14(±4.44)	62.30(±5.29)	0.063 [#]
Gender f (%)			
Male	41(82.0)	42(84.0)	0.790 [*]
Female	09(18.0)	08(16.0)	
BMI (kg/m ²)			
Underweight (<18.5)	01(02.0)	01(02.0)	
Normal (18.5-24.9)	30(60.0)	34(68.0)	
Overweight (25.0-29.9)	19(38.0)	15(30.0)	
Mean(±SD)	24.17(±2.27)	24.26(±2.16)	0.845 [#]
Comorbidities f (%)			
Hypertension	35(70.0)	37(74.0)	0.658 [*]
Diabetes Mellitus	12(24.0)	18(36.0)	0.190 [*]
Heart Failure	03(06.0)	02(04.0)	0.646 [*]
History of Myocardial Infarction	41(82.0)	38(76.0)	0.461 [*]
COPD	07(14.0)	08(16.0)	0.779 [*]

#P value obtained by student's t-test. *P-value obtained by chi-square test.

Table-II
Comparison of perioperative investigations and findings between groups

Preoperative variables	Groups		P-value
	Group A	Group B	
Serum K ⁺ (mmol/L) [mean±SD]	4.11±0.51	3.93±0.47	0.068 [#]
Echocardiography			
LVEF (%) [mean±SD]	58.9±11.7	59.8±11.1	0.674 [#]
Left atrial A-P dimension (mm)[mean±SD]	37.16±3.82	38.36±3.31	0.096 [#]
Coronary Angiogram f(%)			
Single Vessel Disease	05 (10.0)	02 (4.0)	0.269 [*]
Double Vessel Disease	12 (24.0)	18 (36.0)	
Triple Vessel Disease	33 (66.0)	30 (60.0)	
Operative variables			
Total number of grafts (mean±SD)	2.38±0.67	2.40±0.57	0.872 [#]
Duration of surgery (min) (mean±SD)	295.3±24.8	303.0±2+29.9	0.164 [#]
Occurrence of AF (monitor) f(%)	02(04.0)	08(16.0)	0.04 [*]
Peri-operative variables			
ICU stay (days) (Mean±SD)	5.76±1.0	5.46±0.65	0.078 [#]
Post-operative hospital stay(days) (Mean±SD)	10.48±1.07	12.04±1.87	0.037 [#]

#P value obtained by student's t-test. *P-value obtained by chi-square test.

Table-III
Comparison of serum potassium level and occurrence of atrial fibrillation (AF) at postoperative day, at discharge, and after one month between two groups

Postoperative day	Groups		P-value
	Group A	Group B	
Serum Potassium mmol/L (Mean±SD)			
0 POD	4.08±0.44	3.93±0.46	0.100 [#]
1 st POD	4.05±0.48	3.95±0.41	0.244 [#]
2 nd POD	4.15±0.46	3.98±0.51	0.081 [#]
3 rd POD	3.97±0.39	3.99±0.50	0.827 [#]
4 th POD	3.94±0.46	4.01±0.45	0.470 [#]
5 th POD	4.11±0.44	3.94±0.48	0.072 [#]
At discharge	4.15±0.46	4.11±0.55	0.722 [#]
After one month	4.08±0.50	4.10±0.48	0.775 [#]
Occurrence of AF f (%)			
0 POD	2(4.0)	9(18.0)	0.025 [*]
1 st POD	4(8.0)	11(22.0)	0.050 [*]
2 nd POD	4(8.0)	16(32.0)	0.003 [*]
3 rd POD	3(6.0)	15(30.0)	0.002 [*]
4 th POD	1(2.0)	10(20.0)	0.004 [*]
5 th POD	1(2.0)	6(12.0)	0.050 [*]
At discharge	2(4.0)	5(10.0)	0.239 [*]
After one month	1(2.0)	3(6.0)	0.307 [*]

#P value obtained by student's t-test. *P-value obtained by chi-square test.

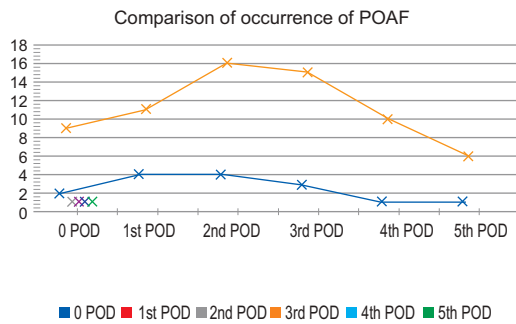


Fig.-2: Occurrence of POAF during the index hospitalization. The occurrence of AF was compared between two groups from the operative day (after arrival at ICU) up to 5th POD by continuous ECG monitor.

Discussion

This present study conducted in the Department of Cardiac Surgery, NICVD, included 100 patients undergoing OPCAB. Half of them were in Group A, preoperatively, and postoperatively on oral omega-3 PUFA, Group A and another half were in Group B, did not on oral omega-3 PUFA preoperatively and post operatively. The purpose of this study was to assess the effect of perioperative oral omega-3 PUFA in preventing atrial fibrillation in patients undergone OPCAB.

In the present study majority of patients in Group A and Group B were in the age group of 61-70 years 78.0% and 60.0%, respectively. Males were predominant in both groups, which were 82.0% and 84.0% in Group A and Group B, respectively. The mean BMI were 24.17 ± 2.27 in group A and 24.26 ± 2.16 in group B. There is no statistically significant difference in terms of age, sex, BMI between the groups. Studies by Calo et al. (2005)²² and Mariscalco et al. (2010)³⁸ also shown similar results.

The risk factors were recorded among the study population. Differences between the two groups for hypertension ($p = 0.658$), diabetes mellitus ($p = 0.190$), heart failure ($p = 0.646$), history of MI ($p = 0.461$) and COPD ($p = 0.779$) were not statistically significant. Calo et al. (2005)²² and Sorice et al. (2011)²⁴ reported similar results in their study. As detected by 12-lead ECG, preoperatively, all the patients in both groups were in sinus rhythm. Preoperative mean \pm SD serum potassium levels were found at 4.11 ± 0.51 mmol/L and 3.93 ± 0.47 mmol/L ($p = 0.068$) in Group A and Group B, respectively. The majority of the patients had triple vessel disease, which was 66.0% and 60.0% in Group A and Group B, respectively, followed by double vessel disease and single vessel. The differences were not statistically significant.

Villareal et al. (2004)³⁹ and a recent review by Sazzad et al (2021)⁴⁰ also found a similar result.

According to the echocardiographic finding, the mean \pm SD of LVEF in Group A and Group B were $58.9 \pm 11.7\%$ and $59.8 \pm 11.1\%$ respectively ($p = 0.674$), and mean \pm SD of left atrial anteroposterior dimension were 37.16 ± 3.82 mm and 38.36 ± 3.31 mm in Group A and Group B, respectively ($p = 0.096$). The differences were not statistically significant. Calo et al. (2005)²² also found similar results, and they reported the mean \pm SD of LVEF were $55.3 \pm 11.4\%$ and $56.3 \pm 12.1\%$ in two groups and mean \pm SD of left atrial anteroposterior dimension in their study were 39.7 ± 5.2 mm and 38.36 ± 5.1 mm in two groups. Mean \pm SD of the number of grafts were 2.38 ± 0.67 and 2.40 ± 0.57 in Group A and Group B, respectively ($p = 0.872$). The mean \pm SD of the duration of surgery was 295.3 ± 24.8 minutes and 303.0 ± 29.9 minutes in Group A and Group B, respectively ($p = 0.164$). The differences were not statistically significant. Per operatively, AF was present in 4.0% patients of Group A and 16.0% patients of Group B ($p = 0.04$). The occurrence of per operative AF between the groups is statistically significant. The occurrence of AF was compared between two groups from the operative day (after arrival at ICU) up to 5th POD by continuous ECG monitor. The results showed significant differences on operative day, after arrival at ICU ($p = 0.025$), 1st POD ($p = 0.050$), 2nd POD ($p = 0.003$), 3rd POD ($p = 0.002$), 4th POD ($p = 0.004$) and 5th POD ($p = 0.050$). The occurrence of AF was also compared between two groups on the day of discharge from the hospital and after one month of discharge by 12-lead ECG. But the differences were not statistically significant at discharge ($p = 0.239$) and one month after discharge ($p = 0.307$). Mariscalco et al. (2010)³⁸ also found similar results.

The mean \pm SD of serum potassium level was compared between two groups from the operative day (after arrival at ICU) up to 5th POD and there were no significant differences on operative day, after arrival at ICU ($p = 0.100$), 1st POD ($p = 0.244$), and 2nd POD ($p = 0.081$), 3rd POD ($p = 0.827$), 4th POD ($p = 0.470$), 5th POD ($p = 0.072$), at discharge ($p = 0.722$) and one month after discharge ($p = 0.775$). The mean \pm SD of total ICU stay was 5.76 ± 1.0 days and 5.46 ± 0.65 days ($p = 0.078$) in Group A and Group B, respectively. The difference was not statistically significant between the two groups. The mean \pm SD of hospital stay after surgery was 10.48 ± 1.07 days and 12.04 ± 1.87 days ($p = 0.037$) in Group A and Group B, respectively. The difference was statistically significant between the two groups. Total ICU stay was

similar between the two groups, but the postoperative hospital stay was shorter in Group A than in Group B, and the difference is statistically significant.

Calo et al. (2005),²² Mariscalco et al. (2010),³⁸ and Langlois et al. (2017)⁴¹ in their study reported similar results of ICU to stay and hospital stay between two groups. Costanzo et al. (2013),⁴² in their meta-analysis of 8 RCTs and 2,687 patients, reported that preoperative supplementation of n-3 PUFA significantly reduces the incidence of POAF by 16% in patients undergoing cardiac surgery, and they also reported that this effect was more pronounced with a 34% reduction in POAF (OR, 0.66; 95% CI, 0.50-0.87; p=0.003) in patients undergoing CABG. But another metaanalysis by Mariani et al. (2013)⁴³, however, reported no significant benefit (OR 0.86; 95% CI, 0.71 to 1.04) with supplementing n-3 PUFA in preventing POAF. Additionally, the occurrence of POAF was similar to Sazzad et al (2018)⁴⁴ and Salekin et al (2019).⁴⁵ Multicenter randomized control trials with a larger sample size among the Bangladeshi population undergone CABG can further generate knowledge regarding this issue that benefits the patient's outcome after cardiac surgery.

Conclusion

This study concluded that perioperative oral omega-3 polyunsaturated fatty acid intake reduces the incidence of postoperative atrial fibrillation in patients undergoing off pump coronary artery bypass graft surgery.

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