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Effects of n-3 polyunsaturated fatty acids on depressive symptoms, anxiety and emotional state in patients with acute myocardial infarction

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Abstract:
Background: Our aim was to assess whether an early introduced n-3 polyunsaturated fatty acids (n-3 PUFA) supplementation affects depression symptoms, anxiety and emotional state in patients with acute myocardial infarction (AMI) and no history of mental disorders.
Methods: Fifty two patients with AMI were enrolled into the study and randomized to the study group (group P; n = 26; standard therapy + n-3 PUFA 1 g daily) or the control group (group C; n = 26; standard therapy). The following psychological tests were used at the baseline (3rd day of AMI) and after one month (30 ± 1 days): Beck Depression Inventory (BDI), State-Trait Anxiety Inventory in a specific situation (STAI-S) and as a general trait (STAI-T), Emotional State Questionnaire (ESQ).
Results: The baseline characteristics, pharmacotherapy and BDI, STAI-S/T and ESQ were similar between both groups. The mean test scores assessed for all patients (group P and C) during the one-month observation were significantly lower for BDI ($p = 0.04$), STAI-T ($p = 0.03$), STAI-S ($p = 0.01$) and harm/loss emotions ($p = 0.005$). After adjusting for age, sex, body mass index, coronary artery disease severity, ejection fraction, serum troponin level and the baseline tests results, n-3 PUFA intervention revealed additional significant decrease in BDI ($p = 0.046$), STAI-S ($p = 0.03$) and harm/loss emotions ($p = 0.04$).
Conclusions: Our study provides novel and preliminary observations – n-3 PUFA supplementation reveals additional decreasing effects on depressive and anxiety symptoms in early post-MI patients.

Key words:
polyunsaturated fatty acids, acute myocardial infarction, depression, anxiety, emotional state

Abbreviations: AMI – acute myocardial infarction, BDI – Beck Depression Inventory, CAD – coronary artery disease, DHA – docosahexaenoic acid, ECG – electrocardiography, EPA – eicosapentaenoic acid, ESQ – Emotional State Questionnaire, n-3 FA – ω-3 fatty acids, n-3 PUFA – ω-3 polyunsaturated fatty acids, STAI – State-Trait Anxiety Inventory, STEMI – ST-elevation myocardial infarction, TTE – transthoracic echocardiography

Introduction

A growing body of evidence suggests a relatively consistent link between psychosocial factors and cardiovascular risk and prognosis in patients after acute myocardial infarction (AMI) [4, 34, 41]. Every fifth

patient with AMI fulfill the criteria for major depression [22]. Anxiety is reported even in 70–80% AMI patients [27]. Despite its prevalence, mood disorders are often unrecognized, neglected or considered to be transient and related to the acute phase. However, even incident depressive symptoms in AMI patients are likely to trigger cardiovascular complications and predict a worse long-term prognosis [13].

ω-3 Fatty acids (n-3 FA) are one of the suggested factors linking mood disorders and cardiovascular complications. Ecological, case-control and cross-sectional studies have showed an inverse relation between fish intake and depression or psychological distress rates [6, 9, 16, 24, 37]. Several effects of n-3 PUFA were observed in secondary cardiovascular prevention [25, 33] and patients after MI are encouraged to increase the amount of n-3 PUFA in their diet or introduce n-3 PUFA supplementation (1 g daily) [11, 41, 43]. However, evidence on the n-3 PUFA effects on mood disorders in AMI patients is scarce and inconsistent.

Our aim was to assess whether an early introduced one-month n-3 PUFA supplementation affects depression symptoms, anxiety and emotional state in patients with AMI and no history of mental disorders.

Materials and Methods

Recruitment and eligibility screening

Patients were recruited and completed the study in the 2nd Department of Cardiology affiliated with the Medical University of Silesia in Katowice, Poland. The study protocol was approved by the local Medical University of Silesia Ethics Committee and all patients submitted written informed consent for the study procedures.

The inclusion criteria were: AMI treated with successful percutaneous coronary intervention with stent implantation, which was defined as optimal coronary flow (Thrombolysis In Myocardial Infarction – TIMI grade 3 complete flow and no local or general complications). AMI was defined according to the guidelines [38, 40, 41] based on clinical symptoms, cardiac markers, electrocardiography (ECG) and transthoracic echocardiography (TTE). All patients were diagnosed for AMI and revealed a rise of creatine phosphokinase-myocardial bound isoenzyme and cardiac troponin I with at least one value above the 99th percentile of the upper reference limit with one or more of the following: typical ischemic symptoms and/or indicative ECG changes and/or new regional wall motion abnormality in TTE. Patients repeated ECG recordings were classified as ST-elevation myocardial infarction (STEMI): new persistent ST-segment elevation or new left bundle branch block or non-ST-elevation myocardial infarction: persistent or transient ST-segment depression, T-wave changes or no significant changes. AMI location was determined according to ECG and/or TTE.

The exclusion criteria included: any cognitive impairment, comorbid psychiatric or neurological disorders, psychosis, substance abuse diagnosed or suspected before, acute and chronic inflammatory diseases (in 3 preceding months), 3rd degree of hypertension according to European Society of Cardiology guidelines, history of myocardial infarction within 6 months prior to the study enrollment, myocarditis and vasculitis, spondyloarthritis, Tietze's syndrome, gastrointestinal tract diseases, diseases of aorta, hormone replacement therapy and underlying malignancies.

All the individuals assessed for eligibility for the study were patients hospitalized for suspected acute coronary syndrome (Fig. 1 – Participant flow). Fifty two patients met the criteria, were enrolled into the study and randomized to the n-3 PUFA group (group P; n = 26; standard therapy + n-3 PUFA 1 g daily) or the control group (group C; n = 26; standard therapy). Patients were allocated to the intervention or control group by the block randomization method using Random Allocation software and a series of numbered sealed envelopes. The patient's allocation was blinded to the investigators performing either baseline or control visit.

None of our participants had been taking n-3 PUFA or other PUFA supplements before. Regular fish consumption before the enrollment was low. The vast majority of patients declared only one fish meal a week without a significant differences between the averages for both groups (Tab. 1).

The clinical characteristics of the study patients is presented in Tables 1–4. Echocardiography was performed in all patients according to the guidelines of the European Society of Echocardiography.

Study design

This study was a randomized, non-placebo, single-center, prospective trial to determine the efficacy of n-3 PUFA 1 g/day added to the standard pharmacotherapy recommended in post-MI patients. The dosage of the study drug was chosen based on the secondary cardiovascular prevention guidelines. The dose range of 1 g daily was evidenced to be safe and affect clinical and preclinical cardiovascular endpoints [28].

Follow-up and treatment adherence

Standard pharmacotherapy following the European Society of Cardiology recommendations was given to all patient: acetylsalicylic acid, clopidogrel, statin, β-blocker and angiotensin converting enzyme inhibitors adjusted to the heart rate and blood pressure. The study drug of highly concentrated n-3 PUFA capsule (Omacor; 1 g/day ω-3-acid ethyl esters = 465 mg eicosapentaenoic acid – EPA + 375 mg docosahexaenoic acid – DHA; Solvay Pharma, Hanover, Germany) was started in the 3rd day of AMI only in the group P and continued once daily thereafter.

All patients were monitored for potential n-3 PUFA adverse effects. Compliance with the study drug supplementation was verified by a capsule count and patients report. All individuals in the group P ingested all doses of the study drug as instructed before enrollment into the study.

Main outcome measures

The following psychological self-reported tests were used at the baseline (3rd day of AMI) and after one month (30 ± 1 days) pharmacotherapy. All have established reliability and were widely used for evaluating outcomes in clinical studies.

Beck Depression Inventory (BDI)

Beck Depression Inventory (BDI) consisted of 21 questions measuring clinical severity of depressive symptoms with four possible answers depending on intensity. A value of 0 to 3 points was assigned for each answer. A total score was a final result for further analysis. The following ranges are usually used: minimal (0–9), mild (10–18), moderate (19–29) and severe depression (30–63) [5].

State-Trait Anxiety Inventory

State-Trait Anxiety Inventory (STAI) was chosen for assessing anxiety in patients. The inventory has forty questions with four possible answers and 1 to 4 points for each question. A total score for two 20-question parts for measuring anxiety in a specific situation (STAI-S) and as a general trait (STAI-T) (Inventory state and trait scores) were determined [21, 36].

Emotional State Questionnaire

Emotional State Questionnaire (ESQ) was used for measuring individual stress symptoms manifestation. ESQ consisted of 15 adjectives determining emotions with possible 1 to 7 points for each question. The emotions were grouped in four classes: ESQ1 – challenge (excitement, satisfaction, enthusiasm); ESQ2 – threat (fear, uncertainty, worry, helplessness); ESQ3 – benefits (contentment, joy, optimism, relief); ESQ4 – harm/loss (anger, disappointment, depression).

Statistical analysis

Baseline characteristics presented in Tables 1–4 are expressed as the means + standard deviation (SD) or number and percentage. The results of BDI, STAI and ESQ are presented in the text showing the means and standard deviation with "p" values for the baseline values and in Table 5 showing the means and 95% confidence intervals with "p" values for the test results after one month. The results' normal distribution was analyzed with the Kolmogorov-Smirnov test. In case of abnormal distribution the logarithmic transformation was used. Baseline clinical parameters and the results of diagnostic tests were compared using the *t*-tests. Categorical variables were compared using the χ^2 test. Repeated measures ANOVA was performed to evaluate the significance of BDI, STAI and ESQ results changes for the whole group (group P and C). The ANCOVA test was used to compare the BDI, STAI and ESQ results between the groups (group P *vs.* C) adjusting for age, sex, body mass index, coronary artery disease severity, ejection fraction, serum troponin level and the baseline tests results. A value of $p < 0.05$ was considered statistically significant. Statistical analysis was performed using the MedCalc, version 10.0.

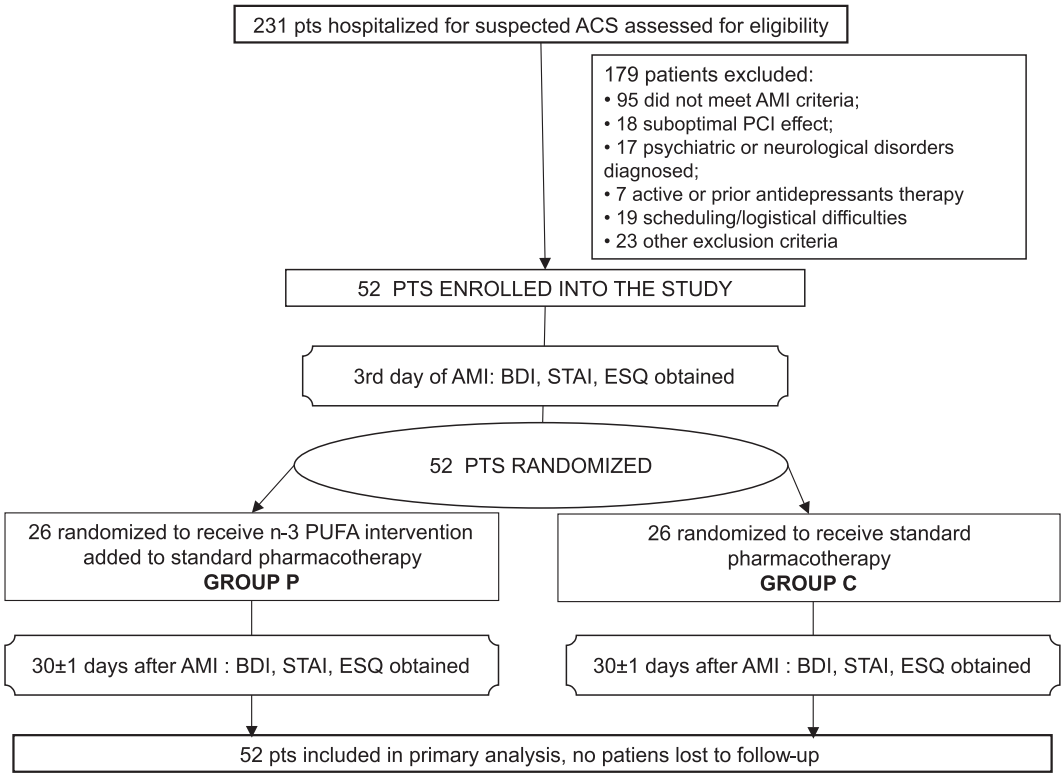

Fig. 1. Participant flow

Tab. 1. Group P (n-3 PUFA) and group C (controls) baseline characteristics

	Group P (n-3 PUFA) n = 26 Mean ± SD or No. (%)	Group C (controls) n = 26 Mean ± SD or No. (%)	p
Age (years)	56.4	59.6 ± 6	NS
Female / Male	3 (13%) / 23 (87%)	4 (18%) / 22 (82%)	NS
Weight (kg)	87.7 ± 12.2	84.7 ± 8.3	NS
Height (cm)	173.2 ± 6.2	171.7 ± 6.3	NS
Waist (cm)	103.3 ± 10.5	102.6 ± 5.7	NS
Hip (cm)	102.6 ± 8.5	100.5 ± 4.7	NS
STEMI / NSTEMI	18 (69%) / 8 (31%)	17 (65%) / 9 (35%)	NS
Anterior wall	8 (31%)	9 (35%)	NS
Inferior wall	11 (43%)	9 (35%)	NS
Lateral wall	4 (15%)	3 (11%)	NS
Undetermined	3 (11%)	5 (19%)	NS
Killip	1.52 ± 0.8	1.42 ± 0.7	NS
Heart rate (bpm)	68 ± 12.0	70.6 ± 11.5	NS
Current smoking	13 (50%)	14 (54%)	NS
Diabetes	5 (19%)	3 (11%)	NS
Fish meals declared	1.15	1.1	NS
Hospital stay (days)	6.1 ± 1.4	6.3 ± 2.4	NS

Results

Baseline parameters

Two hundred thirty one individuals were screened for eligibility criteria and fifty two patients were finally enrolled into the study. None of the patients was lost to follow-up or was withdrawn from the study (Fig. 1: participant flow). There were no significant differences between both groups in baseline demographic, medical, characteristics, echocardiography findings or laboratory tests (Tabs. 1–4).

The baseline tests' scores were not significantly different between the group P and C (the mean ± standard deviation): BDI (11.1 ± 6.8 *vs.* 11.7 ± 6.8; p = 0.35), STAI-T (43.1 ± 8.5 *vs.* 42.6 ± 7.8; p = 0.82), STAI-S (45.1 ± 8.5 *vs.* 43.9 ± 9.4; p = 0.72). The mean scores for all four classes of emotions were comparable between both groups, either: ESQ1 (11.2 ± 3.1 *vs.* 9.9 ± 2.9; p = 0.34), ESQ2 (14.04 ± 5.7 *vs.* 13.4 ± 4.3; p = 0.84), ESQ3 (22.5 ± 5.5 *vs.* 20.4 ± 7.2; p = 0.53), ESQ4 (7.7 ± 2.9 *vs.* 7.1 ± 2.6; p = 0.57).

Main outcomes for all patients during one month observation

The mean scores assessed for all patients (group P and C) during the one month observation were significantly lower for BDI (p = 0.04), STAI-T (p = 0.03), STAI-S (p = 0.01) and ESQ4 (p = 0.005) with no significant change for ESQ1 (p = 0.87), ESQ2 (p = 0.75) and ESQ3 (p = 0.4).

Depression, anxiety, emotions and n-3 PUFA supplementation

After adjusting for age, sex, body mass index, coronary artery disease severity, ejection fraction, serum troponin level and the baseline tests results, n-3 PUFA intervention revealed additional significant influence on the following test scores: BDI (p = 0.046), STAI-S (p = 0.03) and ESQ4 (p = 0.04). However, we found no effects of n-3 PUFA supplementation on the STAI-T (p = 0.94), ESQ1 (p = 0.55), ESQ2 (p = 0.61) and ESQ3 (p = 0.28) (Tab. 5).

Tab. 2. Group P (n-3 PUFA) and group C (controls) baseline characteristics

	Group P (n-3 PUFA) n = 26 Mean ± SD or No. (%)	Group C (controls) n = 26 Mean ± SD or No. (%)	p
Total cholesterol (mg/dl)	204 ± 38.1	194.5 ± 40.3	NS
Triglicerydes (mg/dl)	156.3 ± 56.3	161.3 ± 65.2	NS
High density lipoprotein (mg/dl)	43.1 ± 11.1	41.6 ± 18.1	NS
Low density lipoprotein (mg/dl)	129.7 ± 29.7	120.5 ± 37.1	NS
Creatinine (mg/dl)	0.91 ± 0.23	0.97 ± 0.25	NS
Creatine phosphokinase (U/l)	1199.6 ± 823.3	1115.03 ± 810.2	NS
Creatine phosphokinase-MB (U/l)	144.45 ± 102.1	138.1 ± 98.3	NS
Troponin I (ng/ml)	8.3 ± 7.9	9.1 ± 8.6	NS
Common carotid artery intima media thickness (mm)	0.8 ± 0.2	0.81 ± 0.16	NS
Ejection fraction (%)	55.2 ± 9.7	58 ± 8.8	NS
Mitral valve E wave vel. (cm/s)	73 ± 19	72 ± 13	NS
Mitral valve A wave vel. (cm/s)	62 ± 20	62 ± 17	NS
E/A ratio	1.17 ± 0.3	1.16 ± 0.3	NS
Tissue Doppler Imaging septal mitral annulus motion			
S wave vel. (cm/s)	7.64 ± 2.1	7.85 ± 2.65	NS
E' wave vel. (cm/s)	6.7 ± 1.7	6.7 ± 2.1	NS
A' wave vel. (cm/s)	9.7 ± 2.9	9.3 ± 5.3	NS
E/E' ratio	10.1 ± 3.6	10.7 ± 4.1	NS

Tab. 3. Group P (n-3 PUFA) and group C (controls) baseline characteristics

	Group P (n-3 PUFA) n = 26 Mean ± SD or No. (%)	Group C (controls) n = 26 Mean ± SD or No. (%)	p
Family history of CV events	8 (31%)	11 (42%)	NS
Medical history:			NS
Angina pectoris	17 (65%)	16 (61%)	NS
ACS	6 (23%)	5 (19%)	NS
PCI	4 (15%)	5 (19%)	NS
CABG	2 (7%)	2 (7%)	NS
X-vessel CAD	1.77 ± 0.9	1.89 ± 0.8	NS
PCI in AMI			
LAD	10 (38%)	11(42%)	NS
Cx	4 (15%)	5 (19%)	NS
RCA	12 (46%)	10 (38%)	NS
Qualification for CABG	6 (23%)	6 (23%)	NS

Tab. 4. Group P (n-3 PUFA) and group C (controls) baseline characteristics

	Group P (n-3 PUFA) n = 26 Mean ± SD or No. (%)	Group C (controls) n = 26 Mean ± SD or No. (%)	p
Acetylsalicylic acid	26 (100%)	26 (100%)	NS
Clopidogrel	26 (100%)	26 (100%)	NS
Angiotensin converting enzyme in hibitor	26 (100%)	26 (100%)	NS
β-Blocker	26 (100%)	26 (100%)	NS
Diuretic	8 (31%)	9 (35%)	NS
Calcium channel antagonist	3 (13%)	4 (18%)	NS
Statin	26 (100%)	26 (100%)	NS
Fibrate	2 (8%)	2 (8%)	NS
Nitrate	9 (35%)	7 (26%)	NS

Discussion

The results of our study suggest that low-dose n-3 PUFA supplementation introduced early to standard therapy of AMI reveal some antidepressant and anxiolytic effects in post-MI patients. All patients showed significantly lower depression, anxiety and harm/loss emotion test scores during the observation, which is an expected natural decline in distress symptoms during the recovery from an AMI. The n-3 PUFA intervention showed additional improvement in depression symptoms severity ($p = 0.046$), anxiety intensity assessed as a state ($p = 0.03$) and the intensity of harm/loss emotions ($p = 0.04$). The statistically significant change was not found in all the tests and the clinical significance of mean differences between the groups tests' results may be mild. Both groups had comparable baseline characteristics, results of diagnostic tests and primary AMI treatment. All patients represented a general AMI population with no history of prior mood disorders and standard clinical risk with a relatively mild intensity of depression or anxiety

Tab. 5. BDI, STAI-S, STAI-T and ESQ tests results after one month in the group P (n-3 PUFA) and group C (controls)

Test	Test result after 1 month		Mean difference*	p	95%CI*
	Group P Mean	Group C Mean			
BDI	9.3	11.3	2.02	0.046	0.03-4.0
STAI-S	40.2	44.2	3.91	0.03	0.27-7.55
STAI-T	42.1	41.3	0.79	0.45	–2.91-1.32
ESQ 1	10.36	10.85	0.48	0.55	–1.15-2.12
ESQ 2	13.21	13.82	0.61	0.61	–1.77-2.98
ESQ 3	21.34	22.78	1.44	0.28	–1.23-4.12
ESQ 4	5.37	7.08	1.71	0.04	0.04-3.38

* After adjusting for age, sex, BMI, CAD severity, EF, serum troponin concentration and the baseline test result. BDI: Beck Depression Inventory, STAI-S: State-Trait Anxiety Inventory in a specific situation, STAI-T: State-Trait Anxiety Inventory as a general trait (STAI-T), ESQ: Emotional State Questionnaire, ESQ1 – challenge (excitement, satisfaction, enthusiasm); ESQ2 – threat (fear, uncertainty, worry, helplessness); ESQ3 – benefits (contentment, joy, optimism, relief); ESQ4 – harm/loss (anger, disappointment, depression)

symptoms and stable emotional state evaluated with a widely used and reliable tests. Given the differences in the prevalence of mood disorders between men and women, it is important that our both groups were well sex-matched. Gender as a variable did not change the results of n-3 PUFA intervention. We did not notice any serious clinical events or n-3 PUFA side effects during the observation. Standard medications used in our study patients are not considered to reveal any significant psychiatric effects [18]. Available evidence on psychoactive effects of n-3 PUFA supplementation in an early post-MI patients is very limited. We are not aware of similar randomized clinical studies (study population, intervention and main outcomes assessed), which we may refer our results to.

Acute myocardial infarction, depressive symptoms and n-3 PUFA

Most studies provided a relatively consistent results on inverse relationship between depressive symptoms and n-3 FA levels in a general medical population [6, 16, 17, 19], including patients with AMI [31]. Amin et al. [1] showed that every 4.5% increase in the membrane n-3 FA index was significantly associated with one-point decrease (Patient Health Questionnire-9) in depressive symptoms in patients with confirmed acute coronary syndrome (ACS). Although there are studies suggesting limited or no associations [3], n-3 PUFA deficiency seems to have an important role in the network linking CAD or AMI, depressive symptoms and negative cardiovascular prognosis.

There are several randomized studies evaluating n-3 PUFA supplementation or "fish advice" on depressed mood. The systemic meta-analysis by Appleton et al. suggests a rationale for treatment of diagnosed depression in contrast to prevention in asymptomatic patients with a considerable heterogeneity of analyzed studies [2, 3]. Patients with diagnosed and more-severe depression show beneficial effects of n-3 PUFA (combined mean difference – 0.41) in contrast to small or no effects of n-3 PUFA in mild to moderate depressive symptoms or no evidence of depressed mood. Vast majority of randomized controlled trials were not intended to assess a subpopulation of CAD. The available studies suggest no evidence of n-3 PUFA effects on depression in a non-depressed men with angina pectoris (n = 452) in a six-month observation. However, intervention was based on a fatty fish diet advice or maxepa fish oil supplementation [30]. Although our study patients with no prior history of depression were characterized by a minimal-to-mild depressive symptoms at baseline, due to specific clinical conditions (only CAD patients; early post-infarction period) we cannot compare our results to available clinical trials enrolling patients of similar mood disorder severity, but severely different clinical context.

So far, available studies provide heterogenous conclusions if different forms of treatment of post-MI de-

pression directly improve cardiovascular outcomes, including mortality [12].

Peet and Horrobin [32] and Nemets et al. [29] observed that n-3 PUFA supplementation (1 g or 2 g daily, respectively) significantly improve the efficacy of antidepressant medications based on BDI or Hamilton Rating Scale for Depression in psychiatric patients. However, Carney et al. [7] found, that a ten-week supplementation of n-3 PUFA (2 g daily) added to sertraline treatment (50 mg daily) failed to show superior antidepressant effects of n-3 PUFA compared to placebo in CAD patients with major depression.

Anxiety, mood disorders and n-3 PUFA in acute myocardial infarction patients

Although anxiety is more common in CAD and post-MI patients than depression, evidence on the exact role in cardiovascular prognosis or effective and safe anxiolytic medications is very limited. Only recent studies suggest that anxiety following AMI independently predict the risk of in-hospital adverse events and a long-term clinical outcomes [27]. In contrast to depression, association between other mood psychopathologies and n-3 PUFA are not well established, either. Green et al. showed lower ratio of n-3/n-6 PUFA levels in individuals with anxiety disorders [12]. A few studies of n-3 PUFA intervention provide inconsistent results, including the large study by Ness et al. showing no role for n-3 PUFA in anxiety among angina pectoris men [30]. The majority of studies found some benefits from n-3 PUFA intervention only on selected aspects of mood disorders. However, body of evidence is highly inconsistent and focused on general population or other than CAD subpopulations.

Major potential patomechanisms of n-3 PUFA psychoactive effects in post-MI patients

There are several patomechanisms common for AMI and mood disorders, including: increased proinflammatory cytokines, platelet aggregation and autonomic system dysregulation leading to increased peripheral resistance, arterial hypertension, arrhythmia and hypercoagulability [35]. EPA and DHA decrease the plasma and membrane arachidonic acid level and compete for the cyclooxygenase system [23]. Depression or even a mild negative psychological states (anxiety, anger, confusion) were inversely associated with endothelial dysfunction, dysregulation of the adipokines system, ventricular arrhythmias rate and Heart Rate Variability improvement [8, 10, 15, 26, 39, 42]. However, Kronish et al. demonstrated that depressive symptoms are independent from classical AMI risk factors (GRACE score) and predictors of mortality in depressive disorders following AMI [20]. Therefore, cardiovascular effects of n-3 PUFA may indirectly affect psychological disorders.

Several independent and direct neurophysiological effects on the central nervous system is also considered. N-3 PUFA are essential in physiological processes in cell membrane structure and function, signaling or particular gene expression. EPA and DHA accumulation in synapses is required for serotonergic and dopaminergic functioning [14].

Strenghts and limitations

The strenghts of this prospective and randomized study include a well-defined and matched similar subpopulations of patients with AMI treated according to the current recommendations and the use of standardized psychological assessment. It is possible that higher doses of n-3 FA would be superior in psychoactive effects, however, the dose of n-3 PUFA used in our study follows the secondary prevention recommendations in post-MI patients [41].

We present a non-placebo pilot study with a relatively limited sample size, comparable, however, to most n-3 PUFA supplementation studies. The follow-up was limited to the first month after AMI and the study drug was initiated yet in the 3rd day of general AMI patients. We aimed to assess potential psychoactive effects of n-3 PUFA in early and considered clinically uncertain post-infarction period instead of later secondary prevention. Still, dose, EPA/DHA supplement ratio and minimal time period to first effect are issues to be concerned in further studies. Enrollment of severely depressed AMI patients could have showed better n-3 PUFA effects. However, we aimed to verify another possible effects of n-3 PUFA secondary prevention doses in a post-infarction general population of patients.

Conclusions

Our pilot study addresses an important question and suggests novel and preliminary data on n-3 PUFA effects on depressive symptoms, anxiety and emotional state in post-MI patients. The study provides additional support for further research and a large placebo

controlled randomized controlled trials, including determination of the most suitable dose or EPA/DHA ratio and a target subgroup of patients with a best response to n-3 PUFA.

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Statement of authorship:
MH, KMS, MM, KG carried out the study and drafted the manuscript. KSW, MH, AC participated in the study design and statistical analysis. ZG participated in the study design and coordination. All authors read and approved the final manuscript.

Conflict of interest:
None of the authors have any potential conflict of interest to declare.

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