Original Article

Effects of omega-3 supplementation on quality of life, nutritional status, inflammatory parameters, lipid profile, exercise tolerance and inhaled medications in chronic obstructive pulmonary disease

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Background: The omega-3 polyunsaturated fatty acids (PUFAs) have an anti-inflammatory effect, beneficial for allergies, asthma, chronic obstructive pulmonary disease (COPD), reduce cholesterol and triglyceride levels and blood inflammatory parameters [C-reactive protein (CRP), interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor-alpha (TNF-α)]. The aim of our cross-sectional study was to monitor omega-3 supplementation in patients with severe COPD and assess its association with quality of life, nutritional status, inflammatory parameters, lipid profile, comorbidities, exercise tolerance and inhaled medications.

Methods: Our questionnaire on dietary supplement habits and our validated self-completion questionnaires were filled in by 400 patients with COPD at the National Koranyi Institute of Pulmonology, Hungary, mean age 67 [61–73] years; forced expiratory volume in one second (FEV_1) (ref%): 46 [34–58]; 47.5% male, 52.5% female. We used the disease-specific COPD Assessment Test (CAT) questionnaire to measure quality of life.

Results: More than half of the study participants (61%) did not consume fish or oilseeds at all. Nineteen patients (4.75%) took omega-3 supplementation regularly, mainly on medical advice (0.5 g/day). We observed significantly lower serum CRP levels [6.0 (1–7.3) *vs.* 9.7 (7.4–14.4); P=0.044], more favourable lipid profile [triglycerides, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol] with higher mean body mass index (BMI) [28.1 (22.0–35.3) *vs.* 24.7 (24.5–30.1); P=0.118], better quality of life {CAT: 25 [21–30.5] *vs.* 26 [20–31]; P=0.519}, lower inhaled short-acting bronchodilators use [short-acting beta-agonists (SABAs): 6 (31.58) *vs.* 209 (54.86); P=0.047], lower number of exacerbations in the previous half year [0 (0–1) *vs.* 1 (0–2); P=0.023], and higher 6-minute walking distance (6MWD) {300 [177–387] *vs.* 251 [150–345]; P=0.120} in the group with omega-3 supplementation.

Conclusions: PUFAs are anti-inflammatory and affect the immune system. Our study shows that omega-3 intake of COPD patients is insufficient, and there is an urgent need to develop new anti-inflammatory strategies because only one drug (such as corticosteroids) cannot ease the chronically progressive inflammatory process of COPD.

Keywords: Omega-3; polyunsaturated fatty acid (PUFA); chronic obstructive pulmonary disease (COPD); quality of life; COPD Assessment Test (CAT)

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Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by irreversible airway narrowing and chronic airway inflammation, mainly due to exposure of cigarette smoke (1). COPD causes serious health problems and according to the World Health Organization (WHO) it is the third leading cause of death (2). According to studies cigarette smoke causes harmful airway inflammation before the development of bronchial dysfunction, and this inflammation persists even after smoking cessation (3,4). The main aims of COPD management are to reduce symptoms, slow disease progression, improve exercise tolerance, prevent complications and exacerbations, improve overall health and quality of life and also reduce mortality (5-7).

Although the pathomechanism of COPD is not completely known, researchers believe that oxidative stress may play an important role in molecular mechanisms regulating lung inflammation (8-10). Therefore anti-inflammatory effects of a diet that is rich in antioxidants and polyunsaturated fatty acids (PUFAs) can have an effect on various inflammatory parameters, e.g., C-reactive protein (CRP); interleukin-6 (IL-6); interleukin-8 (IL-8); tumor necrosis factor-alpha (TNF-α), nuclear factor kappa B (NF-κB). By using the benefit of anti-inflammatory effects, COPD progression can be slowed (11,12). In addition to that PUFAs attenuate pulmonary vasoconstriction and pulmonary hypertension caused by hypoxia and altering cell membrane composition (13). Omega-3 PUFA competitively inhibits the metabolism of omega-6 (14), and several studies mentioned its beneficial effects (15-19). One study found that COPD patients, by receiving daily 9.0 g of omega-3 supplementation for eight weeks, increased their physical performance (15). Another study said that the respiratory symptoms of COPD patients improved because of its bronchodilator effect (17). Other studies showed a connection between omega-3 supplementation, weight gain and improved quality of life among COPD patients (18,19).

According to a recommendation of the American Dietetic Association the adequate intake of PUFAs is >0.5 g eicosapentaenoic acid (EPA) + docosahexaenoic acid (DHA) per day (approx. 500–1,000 mg in COPD) (20). Comparing the recommended intake with the daily intake among COPD patients shows that the average of EPA + DHA intake among COPD patients is extremely low [mean ± standard deviation (SD): 0.11±0.21 g; for women: 0.1±0.1 g and for men: 0.12±0.3 g] (17). PUFAs play an important role in regulating inflammatory responses. The current western diet has an omega-6/omega-3 ratio ranging from 20–25/1 compared to the ratio of 1/1 that was prevalent in the diet of our ancestors (21). The PUFA profile of patients can be altered by diet and/or omega-3 supplementation, and various studies suggest that lower intakes of omega-6 and increased intakes of omega-3 can reduce the risk of many chronic inflammatory diseases, including COPD (21-25). In addition, low omega-3 intake is a risk factor for inflammation and deterioration of respiratory function, which is supported by epidemiological and observational studies (22-25). Fan and his colleagues (24) have described that omega-3 modify the fatty acid composition of the T-cell membrane and thus may influence signaling pathways. The results of Varraso and his colleagues (25) have shown that increased fish intake is inversely associated with the risk of developing COPD. All these data suggest that omega-3 PUFAs have anti-inflammatory effects as well as reduce the production of inflammatory markers, all associated with COPD progression. The aim of our present study is to identify COPD patients who take omega-3 essential fatty acid supplementation and to search for and evaluate associations between disease severity, respiratory function, quality of life, comorbidities, physical activity and medication use. The results are intended to help professionals treating COPD patients, to improve the effectiveness of treatments and to highlight the need for intervention in nutritional areas. We present the following article in accordance with the STROBE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-22-254/rc).

Methods

Study design and target population

Data collection was performed with volunteer participants, anonymously, among patients in the Department of Pulmonary Rehabilitation of the National Koranyi Institute for Pulmonology, Budapest, Hungary using self-completed paper-based questionnaires between 1st March, 2019 and 1st March, 2020. Four hundred patients over the age of 40 with COPD participated. The study was cross-sectional and originally planned to include a larger number of patients, but due to the coronavirus pandemic, the study had to be stopped. Inclusion criteria were: age ≥40 years and diagnosis of COPD [post-bronchodilation of forced expiratory volume in one second/forced vital capacity

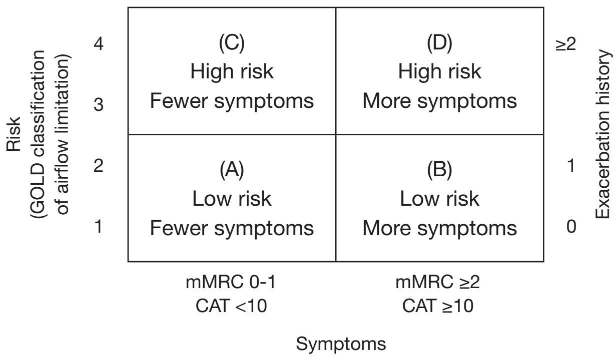

Figure 1 GOLD severity stages of chronic obstructive pulmonary disease. Ref (26): Singh D, Agusti A, Anzueto A, *et al.* Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease: the GOLD science committee report 2019. *Eur Respir J* 2019;53:1900164. https://pubmed.ncbi.nlm.nih.gov/30846476/. GOLD, Global Initiative for Chronic Obstructive Lung Disease; mMRC, the modified Medical Research Council scale; CAT, COPD Assessment Test.

(FEV_1/FVC) <70%]. Exclusion criteria included acute exacerbation, chronic oxygen therapy (resting oxygen saturation less than 89%), history of asthma, lung surgery or severe comorbidities such as severe heart failure or severe liver or kidney failure; acute coronary syndrome or acute cerebrovascular event. The study protocol and the study were approved by the Ethical Committee of the National Koranyi Institute for Pulmonology (25/2017) and the Institutional Review Board of Semmelweis University (TUKEB 44402-2/2018/EKU) in compliance with the Declaration of Helsinki (as revised in 2013). Patients were given oral and written information prior to the assessment, and then they signed a statement of consent. This study is part of a larger one, and the next four questions were added later: (I) in the last six months, have you purchased any prescription or non-prescription food supplements from a pharmacy? (II) Have you taken omega-3 fatty acid supplements (fish oil capsules) regularly in the last six months? (III) If yes, at what dose per day? (IV) If yes, on whose recommendation? (I) Doctor; (II) pharmacist; (III) dietician; (IV) another health professional (e.g., physiotherapist, nurse); (V) friends; (VI) advertisements.

In addition, they also filled in another questionnaire that we wrote, specifically asking about their eating habits, namely: what kind of nourishment do you prefer to eat? Vegetables, fruit, stews, fish, meat, pasta, cakes, oilseeds. What fats do you prefer to use while preparing your food? Sunflower oil, lard, coconut oil, walnut oil, linseed oil or extra virgin olive oil. Have you lost weight/unintentionally gained weight in the last six months? If yes, how much weight have you lost/gained? The questionnaires were administered by a selected coordinator in the Pulmonary Rehabilitation Ward among randomly selected COPD patients, only took about 15 minutes to complete, with the help of a coordinator if necessary. The clinical examination of the patients took place on the same day after they successfully answered the questionnaire. Data on comorbidities, bronchodilator use and number of exacerbations in the previous half year were obtained from the electronic health record system. Participants in the research did not receive any financial, any remuneration or any other allowances.

Assessment of physiological parameters and measurements

Examination of respiratory function

All patients underwent a baseline respiratory function test by automated computerized spirometer for assessing respiratory function. Dynamic lung volumes were defined as the amount of air expelled in the first second [(FEV_1 (ref%)], vital capacity [(FVC (ref%)], the degree of airway obstruction (FEV_1/FVC), inspiratory capacity in liters and percent [(IVC (L), IVC (ref%)], with GLI-defined (Global Lung Function Initiative) normal spirometry (z-score) (26). Patients were graded into GOLD A-D [Global Initiative for Obstructive Lung Disease (international recommendation for COPD)] stages based on current and future risk parameters according to spirometry values, symptoms and exacerbation rate (*Figure 1*) (26).

Quality of life examination

We used the Hungarian validated version of the disease-specific COPD Assessment Test (CAT) (27) to measure quality of life, which provides a comprehensive assessment of the impact of COPD on health. The CAT asks the patient to rate their current symptoms of their disease. The CAT consists of 8 items, each scored between 0 and 5, giving a total score between 0 and 40, with 40 being the worst. A CAT score of ≥10 indicates a significant symptomatic level (GOLD, 2014) (27).

Definition of COPD exacerbation

COPD exacerbation was defined as a significant change of the patient's initial symptoms (dyspnea, cough and sputum production), which is an acute event at a level exceeding the daily variability of symptoms, leading to a change in therapy (26).

The six-minute walk test (6MWT)

During the 6MWT, patients were asked to walk down the aisle for 6 minutes and the maximum walking distance was recorded. 6MWT measures the distance the patient can walk quickly on a hard, flat surface in 6 minutes. This distance value is the result of the test (28).

Body mass index (BMI)

We used an automatic scale to measure body weight and a centimetre tape to measure body height. BMI was calculated by dividing body weight by body height squared (kg/m^2).

Blood tests

We conducted fasting blood tests in the central laboratory of the National Koranyi Institute of Pulmonology and measured the serum CRP with high sensitivity (hs) immunoassay method and the lipid profile (total cholesterine, triglyceride, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol standard method. Patients were in clinically stable condition, without fever and respiratory infection throughout the measurements.

Statistical analysis

All statistical analyses were conducted with STATA SE-20.0. Since most of the continuous data did not follow the normal distribution—verified by Sapphiro-Wilk test, we used non-parametric statistical methods. Continuous variables were represented by medians and interquartile ranges, categorical data were presented with case numbers and proportions. Mann-Whitney tests detected the differences of continuous variables between two groups; frequency differences of categorical variables were examined by Fisher's exact test. All statistical tests were performed at 95% confidence intervals with significance level P<0.05.

Results

The median age of patients (n=400) was 67 [61–73] years, with a sex ratio of 47.5% male and 52.5% female. Median BMI was 25 [21–30] kg/m^2, and median FEV_1 (ref%) was 46 [34–58]. Ever smokers (94.75%) and current smokers (43.5%) smoked an average of 20 cigarettes/day for 40 years. In terms of highest educational attainment, 40% of patients had primary school, 43.5% had secondary school/vocational secondary school/high school and 16.5% had college/university education. *Table 1* shows the comparison and evaluation of COPD patients with and without omega-3 PUFA consumption in terms of lung function and anthropometric parameters.

Nineteen patients (4.75%) took omega-3 supplementation regularly, every day. They bought it at a pharmacy on their doctors' advice and took them at the daily dose recommended by their doctors (0.50 g/day) regularly for past six months. Lower serum CRP levels were measured in patients (n=19) consuming omega-3 fatty acids [IQR 6.0 (1–7.3) *vs.* 9.7 (7.4–14.4); P=0.044], and a more favourable lipid profile (total cholesterol, triglycerides, LDL and HDL cholesterol) with a higher BMI [28.1 (22.0–35.3) *vs.* 24.7 (24.5–30.1); P=0.118], than in patients without omega-3 supplementation (n=381). A lower prevalence of comorbidities (hypertension, ischaemic heart disease, diabetes and psychiatric disorders) was found among patients taking omega-3 PUFAs regularly (see *Table 1*), with a significant difference for ischaemic heart disease. We observed better quality of life {CAT: 25 [21–30.5] *vs.* 26 [20–31]; P=0.519}, lower number of exacerbations in the previous half year [0 (0–1) *vs.* 1 (0–2); P=0.023], higher 6MWT values in the group with omega-3 supplementation (see *Table 1*).

Table 2 lists bronchodilator drugs for COPD patients, divided into omega-3 PUFA consuming and non-consuming groups. Patients who regularly consumed omega-3 fatty acids used fewer inhaled medications, with a significant difference for short-acting bronchodilators use: short-acting beta-agonist (SABA): 6 (31.58%) *vs.* 209 (54.86%); P=0.047.

When asked what they like eating, meat was the most popular choice, followed by vegetables, fruit, pasta, cakes and lastly fish and oilseeds. More than half of the patients (61%) did not eat fish or oilseeds at all. Seventy percent of the participants of the study cooked with sunflower oil and 30% with lard. None of them used extra virgin olive oil, linseed oil or walnut oil. This means that foods rich in omega-3 PUFAs were present in very low proportions in the diets of COPD patients. In addition, patients lost an average of two kg in the last six months (except the group taking omega-3 fatty acids, because they kept their weight).

Discussion

We investigated the clinical value and the anti-inflammatory effects of omega-3 supplementation in COPD patients,

Table 1 Comparison and evaluation of COPD patients with and without omega-3 polyunsaturated fatty acid consumption in terms of lung function and anthropometric parameters

Variables	Omega-3 consumer	Omega-3 non-consumer	P value
Participants (n)	19	381	
Man (n, %)	10 (52.63)	180 (47.24)	0.646
Woman (n, %)	9 (47.37)	201 (52.76)	0.646
Age (year) (IQR)	64.0 [57.5–72.5]	67.0 [61–73]	<0.001
CRP (mg/L)	6.0 [1–7.3]	9.7 [7.4–14.4]	0.044
Smoking status			
Current smokers (n, %)	6 (31.58)	168 (44.09)	0.283
Former smokers (n, %)	12 (63.16)	193 (50.66)	0.287
Never smokers (n, %)	1 (5.26)	20 (5.25)	0.997
Smoking (year)	39 [23–45]	40 [30–47]	0.074
Cigarettes/day	19 [12–21]	20 [15–22]	0.609
BMI (kg/m^2)	28.1 [22.0–35.3]	24.7 [24.5–30.1]	0.118
Total cholesterol (mmol/L)	5.0 [4.5–6.0]	5.1 [4.2–6]	0.920
LDL cholesterol	2.9 [2.2–3.4]	2.9 [2.2–3.5]	0.826
HDL cholesterol	1.5 [1.3–1.8]	1.4 [1.1–1.7]	0.358
Triglycerides (mmol/L)	1.5 [1–1.7]	1.5 [1–2]	0.293
FEV_1 (ref%)	49 [39–56]	46 [34–58]	0.407
FVC (%)	72 [62–86]	70 [58–83]	0.386
FEV_1/FVC (%)	56 [45–60]	51 [42–63]	0.631
GOLD stage (n, %)			
GOLD A	2 (10.53)	28 (7.35)	0.611
GOLD B	7 (36.84)	113 (29.66)	0.504
GOLD C	9 (47.37)	172 (45.14)	0.849
GOLD D	1 (5.26)	68 (17.85)	0.156
Comorbidities (n, %)			
Hypertension	10 (52.63)	275 (72.17)	0.066
Ischemic heart disease	5 (26.31)	195 (51.18)	0.034
Diabetes mellitus	3 (15.78)	68 (17.84)	0.722
Psychiatric diseases	0 (0.00)	47 (12.33)	0.305
CAT (points)	25 [21–30.5]	26 [20–31]	0.519
6MWT (m)	300 [177–387]	251 [150–345]	0.120
Exacerbation (n)	0 [0–1]	1 [0–2]	0.023

Data are presented as median [IQR] or as frequency and percentage. P<0.05 means the two indicators were significantly correlated. COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; BMI, body mass index; LDL, low-density lipoprotein; HDL, high-density lipoprotein; FEV_1, forced expiratory volume in 1 s post-bronchodilator; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; CAT, COPD Assessment Test; 6MWT, six-minute walk test.

Table 2 Inhaled medications taken by chronic obstructive pulmonary disease patients in omega-3 fatty acid consumption and non-consuming groups

Variables	Omega-3 consumer (n, %)	Omega-3 non-consumer (n, %)	P value
Medications (n)	19	381	
SABA	6 (31.58)	209 (54.86)	0.047
LAMA	2 (10.52)	28 (7.35)	0.607
LABA	1 (5.26)	13 (3.41)	0.668
LABA + LAMA	1 (5.26)	23 (6.04)	0.889
ICS + LABA	2 (10.52)	52 (13.65)	0.697
LABA + LAMA + ICS	5 (26.31)	90 (23.62)	0.787
Supplemented with theophylline	6 (31.59)	130 (34.12)	0.819
Combination with leukotriene antagonist	0 (0.00)	3 (0.79)	0.697
No data available	2 (10.52)	42 (11.02)	0.946

P<0.05 means the two indicators were significantly correlated. SABA, short-acting bronchodilators; LAMA, long-acting muscarinic antagonist; LABA, long-acting bronchodilators; ICS, inhaled corticosteroids.

and our results suggest that PUFA intake may be associated with immune function, nutritional status and quality of life. We found that dietary supplementation of PUFAs is positively associated with inflammatory parameters, lipid profile, comorbidities, use of bronchodilator drugs and the number of exacerbations in the previous half year, despite the fact that only a few COPD patients consume them regularly. The recent GOLD recommendation also advises the measurement of a six-minute walk to monitor physical activity to assess the effectiveness of pulmonary rehabilitation, which is a key tool for COPD patients in their management (29). Physical activity strongly predicts mortality in patients with COPD (30). In our study, this parameter was also positively associated with omega-3 fatty acid intake.

In our study, we found lower serum CRP levels in patients taking omega-3 fatty acids regularly, which is consistent with previous studies (31-33). Among the beneficial effects of omega-3 fatty acids, the best known are their inhibitory effects on inflammation and tumour growth, they inhibit the production of prostaglandins and leukotrienes derived from arachidonic acid (ARA) and have antioxidant effects (33). New anti-inflammatory strategies need to be developed because a single drug, including corticosteroids, is unable to slow the chronically progressive inflammatory process of COPD (31). A diet rich in omega-3 fatty acids and supplementation with PUFAs also has anti-inflammatory effects and improves nutritional status and exercise tolerance in patients (32). Nutritional status is particularly important because in the chronic progressive course of COPD, malnutrition impairs quality of life, increases the number and risk of exacerbations, length of hospital stay and health care costs, and low BMI is an independent risk factor for mortality (31-33). Several previous studies have shown that the intake of PUFAs improves the quality of life of patients (15-19,34-38), as COPD is a respiratory and systemic inflammatory disease (36). Omega-3 can slow the inflammatory process and improve quality of life (34-38).

According to researchers, a diet rich in omega-3 fatty acids is "a safe and practical way to treat COPD". A case-control study demonstrated that those who received omega-3 supplementation (0.5–1.0 g/day) had fewer infectious complications and higher six-minute walk distance values (22). Omega-3 fatty acids may affect inflammation by modifying the phospholipid fatty acid composition of cell membranes, altering lipid rafts, or reducing the activation of pro-inflammatory transcription factors, such as NF-κB, and consequentially decreasing the transcription of inflammatory genes (38). The consumption of omega-3 fatty acids as supplements by healthy individuals may reduce inflammatory cytokine levels or may also interfere with the expression of transforming growth factor beta (TGF-β) (39). Omega-3 acids, however, may also have a positive effect on patients with certain lung conditions, such as asthma or COPD (40). Low levels of omega-3

Table 3 The therapeutic potential of omega-3 polyunsaturated fatty acids

No.	Cardiovascular diseases	Inflammatory and metabolic disorders	Neurological disorders
1	Severe hypertriglyceridemia	Type-2 diabetes mellitus	Alzheimer's disease
2	Myocardial infarction	Fatty liver disease	Parkinson's disease
3	Heart failure	Inflammatory bowel disease	Major depression
4	Coronary heart disease	Rheumatoid arthritis	Psychotic disorders
5	Atrial fibrillation	COPD	Cognitive function
6	Atherosclerosis	Macular degeneration	ADHD
7	Blood pressure	Glaucoma	Schizophrenia

COPD, chronic obstructive pulmonary disease; ADHD, attention deficit hyperactivity disorder.

have been associated to the worsening of lung function by affecting a wide array of receptors that play a part in not only inflammation but also the expression of several genes (38-40). Conversely, increased intake of omega-3 fatty acids may exert a positive effect on the functioning of the immune system and thus play an important role in the prevention and management of COPD (41,42). Moreover, fatty acids, such as EPA or DHA, also decrease the production of certain mediators, such as leukotriene B4 (LTB4) and prostaglandin E2 (PGE2) (38). These results point in the direction that omega-3 essential fatty acids may play an important part in the tertiary prevention of COPD as well.

Eating seafood and oilseeds are highly recommended. The diet of the Hungarian population typically consists of high total fatty acid consumption (over 40%), high saturated fat and low polyunsaturated fat consumption, overweight and especially obesity rates have increased significantly, which is also a major public health problem (43-45). Dietary guidelines recommend that 20 to 30 percent of daily energy intake should be in the form of fat, mainly PUFAs (46). Omega-3 can be found in some vegetable oils (e.g., rapeseed oil, linseed oil), in domestic fish (e.g., busa), and in oilseeds (e.g., walnuts, almonds) and oils made from them. The ideal would be to eat fish two or three times a week, a handful of nuts, almonds and other unsalted oil seeds at least three times a week. However, the Hungarian population tends to bake with sunflower oil, while they have no real culture in eating any fish or oilseeds, so their diet is more high in omega-6 fatty acids rather than the beneficial, anti-inflammatory omega-3 (47). While dietitians recommend a ratio of 1:3 to 1:5 for omega-3 and omega-6 fatty acids, the latest survey on national dietary habits found that the ratio is 1:30 in Hungary (47). It should be pointed out how fish consumption is limited here, in our country (about 2.5–3 kg fish/person/year). So generally speaking, Hungarians suffer from a lack of omega-3 essential fatty acids (47).

The human body is not capable of biosynthesising essential fatty acids because it does not have the enzymes to form a double bond at the omega-3 or omega-6 position. Therefore, we need to receive these essential fatty acids from food or supplementation. Daily consumption of olive oil provides the monounsaturated omega-9 fatty acids, while the regular intake of seafood and nuts provides essential polyunsaturated omega-3 fatty acids. Based on research findings the beneficial nutritional and dietary effects of the Mediterranean diet are attributed to the combination of dietary components (48). It is also important to note that fatty acids can be grouped by their carbon chain length into short, medium and long-chain fatty acids. A short type is, e.g., butyric acid, an example of the medium, is capric acid and palmitic acid is one of the long types. A distinction is made between saturated (e.g., coconut oil) and unsaturated fatty acids, which can be monounsaturated (e.g., olive oil) or polyunsaturated (e.g., fish oil, linseed oil). The question may arise as to which to consume regularly and in what proportions. Eating fish twice/three times a week or 1 teaspoon of flaxseed oil a day should cover your omega-3 intake; Olive oil, linseed oil, and walnut oil should be eaten raw, e.g., in salads (49). Among these fatty acids, omega-3 and omega-9 PUFAs seem to be the most important, due to their multiple biological roles, such as reducing the oxidative stress, influencing the inflammatory cascade, presenting cardiovascular protection and neuroprotection (49). For the therapeutic potential of omega-3 PUFAs in various diseases, see *Table 3*.

Studies indicate that as a result of the Western diet, the human cell membrane may contain higher levels of both omega-6 and ARA, an important substrate for the production of eicosanoids (50-52). As a result of certain enzymes, such as cyclooxygenase, lipoxygenase, and cytochrome P450, eicosanoids are produced from ARA. Eicosanoids not only recruit inflammatory cells in the lungs but also affect the smooth muscle contraction and the peroxidation of lipids (50-52). Omega-3 fatty acid consumption decreases the production of eicosanoids and parallel to this increases the level of EPA and DHA of cells, modifies the composition of cell membranes, prevents the activation of pro-inflammatory mediators and thus may improve the condition of patients with COPD (52).

Our study investigated the clinical value and anti-inflammatory effects of omega-3 supplementation in COPD patients, and our results suggest that PUFA intake may be associated with quality of life. We also found out that PUFA supplementation was positively associated with nutritional status, exercise tolerance, inflammatory parameters, lipid profile, bronchodilator use and the number of exacerbations in the previous half year. Our results showed that although patients taking omega-3 supplements had better clinical outcomes, e.g., six-minute walk distance or number of exacerbations in the previous half year, our assessment may not be correct. It is possible that these patients are more health conscious, have better access to regular medical care, visit their doctor more often and are more cooperative with treatment, hence improving health parameters. We would also note that the number of omega-3 supplement users in our sample was very low, only 4.75%, making it difficult to draw any conclusions from the data. Furthermore, the higher BMI observed in the omega-3 supplement group may be beneficial in COPD, especially in respiratory function and exercise tolerance, but excess weight increases chronic inflammation, which may also have attenuated our results. Therefore, it would also be beneficial to perform a body composition analysis, which would provide specific information on the body fat percentage and muscle percentage of patients. In conclusion, PUFAs play an important role in the regulation of inflammatory processes, and omega-3 fatty acid supplements may reduce inflammation in COPD.

Limitations of the study

The disadvantage of our study is that it was a cross-sectional observational study, the cause and effect relationship is not clear. Despite our observation that PUFA intake is associated with a better lipid profile, better nutritional status and better quality of life in patients with COPD, further randomised controlled, follow-up studies are needed to clarify the health-related benefits of PUFAs. Further studies on the effect of high-dose omega-3 supplementation in the management of COPD may be of interest.

Conclusions

We examined the prevalence of PUFA intake among COPD patients and found that PUFA supplementation is positively associated with nutritional status, quality of life, inflammatory parameters, respiratory medication intake and exacerbation rates, yet very few patients take them regularly (4.75%). Our observational data support the hypothesis that omega-3 fatty acid supplementation may be an effective anti-inflammatory strategy in the management of COPD. Our results can be considered as preliminary finding, i.e., regular supplementation of omega-3 PUFAs may help COPD patients to improve their quality of life.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-22-254/rc

Data Sharing Statement: Available at https://apm.amegroups.com/article/view/10.21037/apm-22-254/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-22-254/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study protocol and the study were approved by the Ethical Committee of the National Koranyi Institute for Pulmonology (25/2017) and the Institutional Review Board of Semmelweis University (TUKEB 44402-2/2018/EKU) in compliance with the Declaration of Helsinki (as revised in 2013). Patients were given oral and written information prior to the assessment, and then they signed a statement of consent.

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