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ORIGINAL ARTICLE

# Abnormal fatty acid distribution of the serum phospholipids of patients with non-Hodgkin lymphoma

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**Abstract** The data about the fatty acid (FA) status of non-Hodgkin lymphoma (NHL) patients are poor. Therefore, the aim of this study was to investigate the FA profile of serum phospholipids in NHL patients related to the aggressiveness and clinical stage of NHL. We analyzed the FA profile of serum phospholipids in 47 newly diagnosed, untreated NHL patients and in 29 healthy subjects. Significantly higher ($p<0.001$) levels of palmitic (16:0), oleic (18:1 n-9) and arachidonic acids (20:4 n-6), saturated and monounsaturated FA were found in NHL patients, while linoleic acid (18:2 n-6) and the levels of total polyunsaturated FA (PUFA), n-3 PUFA, eicosapentaenoic (20:5 n-3) and docosahexaenoic (DHA, 22:6 n-3) were significantly reduced ($p<0.01$). The level of oleic acid in patients with indolent NHL was significantly lower ($p<0.05$) than in more aggressive types of disease. Contents of palmitoleic acid, docosatetraenoic (22:4 n-6), and PUFA was lower in very aggressive NHL. According to clinical stage (CS), patients with CS I had significantly higher SFA and lower n-6 FA than other three groups, and group with CS IV showed significantly decreased DHA and n-3 PUFA. Our results showed an abnormal FA profile in serum phospholipids in NHL patients.

**Keywords** Fatty acids · Serum phospholipids · Non-Hodgkin lymphoma

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## Introduction

Incidence and mortality rates of non-Hodgkin lymphoma (NHL) have greatly increased during the past several decades [1]. Nevertheless, the factors that could have played a role to these upward trends are still unclear, including potential impact of the diet. The mechanisms through which diet may influence the development of NHL are unknown, but it has been shown that increased risk of NHL has been related to animal proteins [2] and total fat intake [3, 4], mainly saturated and monounsaturated fat intake [3, 4] whereas polyunsaturated fat showed a protective effect [2, 5]. Particularly dietary polyunsaturated fatty acids of the n-3 series (n-3 PUFA) have shown a protective effect against many cancers. The intake of even relatively small amounts of fish rich in n-3 PUFA is a favorable indicator of the risk of several digestive tract cancers, notably colon and rectal cancer [6, 7]. In a very large case-control study, Fritschi et al. [8] have found a strong protective effect of fresh fish intake for leukemia, myeloma and NHL. It is also known that essential n-3 and n-6 fatty acids (EFA) may participate in the aetiology of

some types of cancer [9]. Recently Crowe et al. [10] reported that plausible biological mechanisms underlie possible associations between fatty acids (FA) in blood, representing dietary intake, and risk of prostate cancer. However, studies reporting the FA status of cancer patients are rare. Women with higher 18:0/18:1 fatty acid ratio in the blood were shown to be at higher risk for breast [11] and cervical cancer [12]. Van Leeuwen et al. [13] studied patients with lung, esophageal or pancreatic cancer and found reduced plasma n-3 PUFA levels in pancreatic patients compared with the control group, and suggested that plasma FA composition may vary among different types of cancers. Indices of FA status may have prognostic value for selecting patients likely to obtain benefits from supplementation, as well as for assessing the efficacy of supplementation protocols [14].

Considering the lack of information on FA status in NHL patients and given the potential therapeutic possibilities of these essential nutrients, the aim of this study was to investigate the serum phospholipids fatty acid composition of untreated NHL patients, in order to examine their relationship with the established disease, aggressiveness and clinical stage of NHL.

## Patients and methods

The total of 47 adult patients with histologically confirmed NHL— 26 male and 21 female, median age 57 years (range, 19–74 years of age), from Department of Hematology Clinical Hospital Center Zemun, Belgrade, entered this study. They were recruited consecutively from June 2007 to March 2008. None of the patients had other malignant or serious non-malignant chronic disease, including diabetes, and none of them received lipid lowering drugs, beta-blockers, hormone therapy, or cytostatics in the 3 months prior to joining the study. After lymph node biopsy or biopsy of primary extranodal site, histological diagnosis was made according to the Revised European-American Lymphoma classification/World Health Organization classification [15]. Tumors classified as NHL represent several distinct morphologic and histologic entities with different prognoses and responses. The patients were divided according to NHL subtypes into three groups: group I, the patients with indolent, i.e., low-risk NHL ($n$=15); group A, the patients with aggressive, i.e., intermediate risk NHL ($n$=23); and group VA, a very aggressive disease, i.e., high-risk NHL ($n$=9). The clinical stage of disease was defined as proposed by the Ann Arbor Conference [16]: Clinical stage I (CS I), six patients; Clinical stage II (CS II), ten patients; Clinical stage III (CS III), 13 patients; and Clinical stage IV (CS IV), 18 patients.

The control group was established of 29 healthy persons, 15 men and 14 women, median age 53 years (range, 23–71 years of age), drawn from medical staff. Exclusion criteria for the healthy subjects were a history of malignant disease or myocardial infarction, and the presence of diabetes, unstable angina pectoris, active liver disease and hepatic or renal dysfunction. Characteristics of study participants are presented in Table 1.

The subjects completed a questionnaire on their eating habits under supervision of a trained nutritionist. No significant qualitative and quantitative differences were recorded among the groups regarding their eating habits. All patients and control subjects in our study had low habitual consumption of foods containing soy, fish intake once a week and no dietary supplementation of oil rich in long-chain fatty acid (fish, sesame, or linseed oil) as determined by diet assessment made at the time of recruitment.

All study participants provided written informed consent which was approved by the Ethical Review Boards of the

**Table 1** Study participants' characteristics

| | *NHL* patients | Control subjects |
|---|---|---|
| No (M/F) | 47 (26/21) | 29 (15/14) |
| Age (years) | 57 (19–74) | 53 (23–71) |
| Clinical stage (No) | | |
| CS I | 6 | |
| CS II | 10 | |
| CS III | 13 | |
| CS IV | 18 | |
| Triglycerides(mmol/l) | 1.5±0.3 | 1.4±0.3 |
| Total cholesterol (mmol/l) | 3.6±0.6* | 5.3±0.6 |
| LDL-cholesterol (mmol/l) | 2.2±0.4** | 3.8±0. 6 |
| HDL-cholesterol (mmol/l) | 1.0±0.2* | 1.2±0.3 |
| Total phospholipids | 2.2±0.3* | 2.9±0.4 |

*$p$<0.01; **$p$<0.001

participating institutions in accordance with the principles of the Declaration of Helsinki.

### Fatty acid determination

Blood samples were collected in the morning after 12 h fast, 1 day after initial diagnosis of NHL. Serum samples were used immediately for biochemical analysis, and for analysis of FA composition serum was frozen. Cholesterol and triglyceride concentrations were measured in serum using the automated enzymatic methods (EliTech Diagnostic, Sees, France). The total phospholipid (PL) concentration in serum was determined by the Zilversmit method [17].

Serum lipids were extracted with chloroform: methanol mixture (2: 1*v*/*v*) by Sperry and Brand method [18]. Serum phospholipids (PL) were separated by one-dimensional thin-layer chromatography (TLC) in a neutral lipid solvent system petrol ether-diethyl ether-acetic acid (87:12:1, *v*/*v*/*v*) using Silica Gel GF plates (C. Merck, Darmstadt, Germany).

Methyl esters of phospholipids FA were prepared by methods that have already been reported [19], with 2,6-di-tert-butyl-4-methylphenol (BHT) added as an antioxidant. Fatty acid methyl esters derivatives were analyzed by gas chromatography using Varian GC (Model 3400, Varian Associates) equipped with DB-23 (30 m×0.53 mm i.d., film thickness 0.5 μm, J&W Scientific Inc Bellefonte, Folsona, CA, USA) fused silica capillary column. Analysis was performed in duplicate for each sample. Individual FA methyl esters were identified by comparing peak retention times with authentic standards (SigmaAldrich, Germany) and/or the PUFA-2 standard mixtures (Supelco Inc., Bellefonte). The results were expressed as the relative percentage of total identified fatty acids. In addition, several fatty-acid indexes, reflecting desaturase and elongase activity, were derived from the primary data. The ratios of 20:4/20:3, 20:3/18:2 and 22:6/22:5 were used as a measure of estimated delta-5-desaturase, delta-6-desaturase and delta-4-desaturase activities respectively, while 18:1/18:0 and 18:0/16:0 ratios represented estimated delta-9-desaturase and elongase activities [19, 20].

### Statistical analysis

All the results are expressed as the mean±SD. Normality was tested using the Shapiro–Wilk's test. One-way ANOVA, followed by the Tukey's post-hoc test, and the Student *t* test were used to compare the normally distributed variables, and nonparametric Kruskal–Wallis test and Mann–Whitney *U* test for non-normally distributed variables analysis (16:1, 20:5 and SFA/UNSFA ratio). The differences were considered significant at $p \leq 0.05$.

## Results

Serum phospholipid fatty acids composition in NHL patients is shown in Table 2. These results indicate significant difference in all serum phospholipid FA in NHL patients when compared with the control subjects. Significantly higher ($p<0.001$) levels of palmitic (16:0) and oleic (18:1 n-9) acids, led to significantly higher levels of saturated (SFA) and monounsaturated fatty acids (MUFA) in NHL patients, despite of their having significantly lower stearic (18:0) and palmitoleic (16:1 n-7) acid than those found in healthy subjects. The levels of total PUFA, n-3 PUFA, eicosapentaenoic (EPA, 20:5 n-3), docosahexaenoic (DHA, 22:6 n-3), and docosapentaenoic acids (DPA, 22:5 n-3) in NHL patients was significantly reduced ($p<0.05$), while PUFA from n-6 series dihomo-γ-linoleic acid (DGLA, 20:3 n-6), arachidonic acid (AA, 20:4) and docosateraenoic acid (22:4 n-6) were significantly higher ($p<0.001$) than in control group. However, level of linoleic acid (LA, 18:2 n-6) was significantly decreased in patients ($p<0.001$), causing lower total n-6 PUFA when compared with healthy participants as well. Total SFA/UNSFA ratio, SFA/PUFA and n-6/n-3 ratio were significantly higher ($p<0.01$) in patients with NHL than in control group.

The estimated activities of desaturase system were also changed: the Δ6 and Δ9 desaturase had significantly increased activity ($p<0.001$) in NHL patients, whereas Δ4 and Δ5 desaturases and elongase showed significantly decreased function ($p<0.01$, $p<0.05$, and $p<0.01$, respectively) in the patients than in healthy individuals. Regarding that FA profile of serum PL was markedly different in patients with NHL compared with healthy subjects, we further determined possible differences among NHL patients according to aggressiveness and clinical stage of the disease. The obtained results are presented in Tables 3 and 4, respectively.

The level of oleic acid in patients with indolent form of disease (I) was significantly lower ($p<0.05$) than in patients with aggressive (A) and very aggressive (VA) NHL. Group VA had significantly lower concentrations of palmitoleic acid, docosatetraenoic (22:4 n-6) and PUFA, with a significantly elevated ratio of SFA/UNSFA and SFA/PUFA than groups I and A (Table 3). Lower levels of DPA (22:5 n-3) and n-6 PUFA and higher palmitic acid were also found in patients with VA NHL when compared with other two groups, but these differences were non-significant. There were no significant differences in estimated desaturase and elongase activity relating to aggressiveness of NHL as well.

According to clinical stage, NHL patients were divided in four groups (CS I-IV). Patients with CS I ($n=6$) had significantly higher SFA and SFA/PUFA ratio and lower n-6 FA than other three groups of patients. Group with the

**Table 2** Fatty acid composition (mol.% of total) of serum phospholipids in patients with non-Hodgkin lymphoma (NHL patients) and healthy subjects (Control group)

| FA | NHL patients ($n$=47) | Control group ($n$=29) |
|---|---|---|
| 16:0 | 30.2±3.5*** | 26.4±2.5 |
| 18:0 | 14.4±1.5** | 15.9±1.9 |
| 16:1 n-7 | 0.1±0.2*** | 0.8±1.1 |
| 18:1 n-9 | 13.8±1.4*** | 11.7±1.5 |
| 18:2 n-6 | 20.0±2.4*** | 25.9±3.5 |
| 20:3 n-6 | 3.9±1.0*** | 2.7±1.0 |
| 20:4 n-6 | 14.3±1.5*** | 11.2±2.0 |
| 20:5 n-3 | 0.2±0.1* | 0.3±0.2 |
| 22:4 n-6 | 0.6±0.2*** | 0.3±0.2 |
| 22:5 n-3 | 0.4±0.2** | 0.6±0.1 |
| 22:6 n-3 | 2.1±0.68*** | 3.6±1.1 |
| SFA | 44.9±2.1** | 42.5±4.4 |
| MUFA | 13.9±1.3*** | 12.0±1.8 |
| Σ n-6 | 38.8±2.6* | 40.4±3.9 |
| Σ n-3 | 2.7±0.7*** | 4.5±1.3 |
| PUFA | 41.7±2.7*** | 44.9±4.3 |
| n-6/n-3 | 15.4±4.6*** | 9.6±2.3 |
| SFA/UNSFA | 0.8±0.0*** | 0.7±0.1 |
| SFA/PUFA | 1.1±0.1** | 0.9±0.2 |
| 20:4/20:3 (Δ5) | 3.9±1.2* | 4.7±1.9 |
| 20:3/18:2 (Δ6) | 0.2±0.1*** | 0.1±0.1 |
| 22:6/22:5 (Δ4) | 5.4±1.6** | 6.6±2.3 |
| 18:1/18:0 (Δ9) | 1.0±0.2*** | 0.8±0.1 |
| 18:0/16:0 (elongase) | 0.5±0.1** | 0.6±0.1 |

*$p$<0.05; **$p$<0.01; ***$p$<0.001

last stage, CS IV, showed significantly decreased DHA and total n-3, and elevated DGLA and n-6/n-3 ratio compared to patients with CS I-III. Oleic acid and MUFA demonstrated an increasing trend in CS I-IV, and AA was the highest in CS IV, but these changes were not significant. Patients with CS I had significantly higher estimated activity of Δ5 desaturase compared with other groups, while Δ6 and Δ9 desaturase exerted significantly increased activity in patients in fourth CS than in patients with CS I-III and CS I-II, respectively (Table 4).

## Discussion

We made the first comprehensive assessment of serum PL fatty acids in a mixed group of NHL patients, divided according to clinical stage and aggressiveness of the cancer. We observed altered content of FA in serum PL and altered estimated activity of desaturase system in NHL patients compared with healthy subjects, but also differences in FA profiles depending on clinical stage or aggressiveness.

NHL represent a diverse group of hematologic cancers, and among many different divisions, we grouped the patients according to clinical stage and aggressiveness since we previously found significant differences in serum lipid profiles and total phospholipids of NHL patients divided in this way [21]. Abnormalities of serum lipid profiles of cancer patients compared with healthy individuals have often been reported [22–24]. Our group reported recently low plasma PL concentration in a group of NHL patients [21]. Furthermore, Murphy et al. [25] demonstrated that low plasma level of PL had been associated with approximately twofold shorter survival in cancer patients, giving this parameter a prognostic significance.

Plasma PL contain the majority of essential FA in blood, reflect overall metabolism of endogenous and dietary FA and can be used to detect aberrations in n-6 and n-3 essential FA metabolism [25]. NHL patients involved in our study were found to have increased contents of SFA and MUFA and very low proportions of long chain PUFA (both n-6 and n-3 series) in serum PL. In addition, their n-6/n-3 FA ratio was significantly higher (15.4) than in healthy individuals (9.6). The similar results were reported by Pratt et al. [14] in serum and neutrophil PL of patients with advanced cancer. It is not clear whether altered diet or altered metabolism of FA would account for these differences, nor is it known to what extent the disease might have contributed, but the effect of therapy in our study is excluded, since all patients were recruited before the initiation of the treatment. The long chain n-3 PUFA, EPA

**Table 3** Fatty acid composition (mol.% of total) of serum phospholipids in NHL patients divided according to the aggressiveness of NHL

| FA | I ($n$=25) | A ($n$=23) | VA ($n$=9) |
|---|---|---|---|
| 16:0 | 29.7±1.8 | 29.9±4.3 | 32.1±3.1 |
| 18:0 | 14.7±2.1 | 14.2±1.2 | 14.3±1.3 |
| 16:1 n-7 | 0.4±0.3 | 0.3±0.2 | 0.3±0.1 |
| 18:1 n-9 | 13.0±1.6 | 14.1±1.0* | 14.4±1.5* |
| 18:2 n-6 | 21.2±2.3 | 19.7±2.1 | 18.9±2.9 |
| 20:3 n-6 | 3.9±1.1 | 4.0±0.9 | 3.5±1.3 |
| 20:4 n-6 | 14.2±1.5 | 14.3±1.4 | 14.6±1.8 |
| 20:5 n-3 | 0.2±0.1 | 0.2±0.1 | 0.2±0.1 |
| 22:4 n-6 | 0.6±0.2 | 0.6±0.1 | 0.4±0.2**,### |
| 22:5 n-3 | 0.4±0.1 | 0.4±0.2 | 0.3±0.2 |
| 22:6 n-3 | 2.1±0.5 | 2.2±0.6 | 2.0±0.6 |
| SFA | 44.4±1.3 | 44.7±1.5 | 46.5±3.7 |
| MUFA | 13.4±1.5 | 14.1±1.0 | 14.5±1.5 |
| Σ n-6 | 39.8±1.5 | 39.0±2.3 | 36.5±3.4 |
| Σ n-3 | 2.7±0.6 | 2.8±0.8 | 2.6±0.87 |
| PUFA | 42.6±1.4 | 41.8±2.4 | 39.8±4.2* |
| n-6/n-3 | 15.5±3.4 | 15.4±5.6 | 15.0±4.0 |
| SFA/UNSFA | 0.8±0.1 | 0.8±0.0 | 0.9±0.1*,## |
| SFA/PUFA | 1.0±0.1 | 1.1±0.1 | 1.2±0.2**,# |
| 20:4/20:3 (Δ5) | 3.8±0.8 | 3.7±0.9 | 4.8±2.1 |
| 20:3/18:2 (Δ6) | 0.2±0.1 | 0.2±0.1 | 0.2±0.1 |
| 22:6/22:5 (Δ4) | 4.9±1.3 | 5.6±1.9 | 5.5±1.1 |
| 18:1/18:0 (Δ9) | 0.9±0.2 | 1.0±0.1 | 1.0±0.2 |
| 18:0/16:0 (elongase) | 0.5±0.1 | 0.5±0.2 | 0.5±0.1 |

*I* indolent NHL, *A* aggressive and *VA* very aggressive NHL

*$p$<0.05; **$p$<0.01 when compared with group I. #$p$<0.05; ##$p$<0.01; ###$p$<0.001 when compared with group A

and DHA are thought to have cancer-protective effects, partly due to competitive inhibition of the use of AA (n-6 20:4), for the production of eicosanoids which have been associated with tumor promotion and progression [26, 27]. A ratio of n-3/n-6 FA intake >0.5 may be important in reducing cancer risk; however, Western diets tend to result in a much lower ratio [8, 27]. Population studies illustrate the large variation of n-3 levels in blood and cell lipids in individuals from different countries and regions [27, 28], but our patients and control subjects did not differ significantly in types or quantities of consumed food and beverages. PUFA n-3 series may also up-regulate anticancer defense such as natural killer cell cytotoxicity and humoral and T cell responses [29]. One of the most striking features of the FA profiles of our patients was low proportions of EPA and DHA, with very high n-6/n-3 ratio in serum PL, particularly in CS IV. It is of a great importance since a decreased n-6/n-3 FA ratio reduces the invasion potential of human lung cancer cells by probably downregulating the cell adhesion/invasion-related molecules, suggesting a role for the ratio of n-6 to n-3 FA in the prevention and treatment of cancer [30]. In addition, n-3 FA were shown to be particularly depleted prior to death in cancer patients: alpha-LA was 59% lower and the longer chain EPA and DHA were 26% and 40% lower in patients surviving less than 238 days versus those surviving longer [25]. Thus the authors proposed prognostic value of n-3 FA in cancer patients.

On the other hand, AA percentage in serum PL of the patients was higher than in control subjects, but it was independent on the aggressiveness or CS, although patients with CS IV had slightly higher content of AA than other groups. Our observations are in line with previously reported data [31, 32]. AA percentage in serum PL is often elevated not only in cancer, but also in cardiovascular disease, hyperlipidemia, etc. [33].

Reduced level of stearic acid and increased level of oleic acid have been reported for patients with cancers at different sites [11, 34, 35]. We found significantly decreased content of stearic acid and increased oleic acid in NHL patients and these alterations followed clinical stages and aggressiveness of the disease, although we have to emphasise a small number of patients in certain subgroups (CS I $n$=6, VA $n$=9, etc.). Stearic acid inhibits in vitro proliferation of various human cancer cell lines [36]. A possible interpretation is that stearic acid is directly involved in the inhibition of tumor development [11]. Also, Polesel et al. [5] provided convincing evidence on a protective effect of PUFA, in particular of linoleic acid, on NHL risk. In accordance to these findings, our NHL patients had significantly reduced content of LA, particularly in CS IV and in more aggressive forms of the cancer.

Alteration in dietary fat intake as well as level of saturation was found to alter membrane phospholipid FA composition in a variety of cellular and subcellular membranes. Saturated fat was associated with a significantly increased risk of diffuse lymphoma, B-cell lymphoma, and intermediate/high-grade lymphoma [37, 38]. Both SFA/UNSFA and SFA/PUFA ratios were significantly higher in NHL patients involved in our study compared with healthy individuals, as well as in patients with very aggressive compared with indolent and aggressive type of NHL. The possible cause could be the overexpression of the enzyme fatty acid synthase (FAS) in NHL cells, which is responsible for de novo synthesis of medium and long chain SFA [39]. Elevated FAS activity has been identified in many malignancies increasing the ratio of SFA/UNSFA [12, 40], particularly in aggressive types. The increased SFA/UNSFA ratio may be an indirect marker of FA metabolism dysregulation in NHL and other cancer patients and a potential selective target for antineoplastic therapy.

**Table 4** Fatty acid composition (mol.% of total) of serum phospholipids in NHL patients divided according to clinical stage (CS I-IV) of NHL

| FA | CS I ($n$=6) | CS II ($n$=10) | CS III ($n$=13) | CS IV ($n$=18) |
|---|---|---|---|---|
| 16:0 | 32.6±3.9 | 29.3±1.3 | 28.6±5.3 | 31.2±2.0 |
| 18:0 | 15.6±1.3 | 15.2±1.5 | 14.5±1.3 | 13.5±1.3*,## |
| 16:1 n-7 | 0.3±0.4 | 0.2±0.2 | 0.1±0.2 | 0.1±0.2 |
| 18:1 n-9 | 12.9±1.7 | 13.5±1.2 | 14.0±1.2 | 14.1±1.5 |
| 18:2 n-6 | 20.4±5.0 | 21.4±1.6 | 20.3±1.9 | 18.9±1.8# |
| 20:3 n-6 | 2.6±1.0 | 3.6±0.8 | 3.6±0.6 | 4.6±1.0***,#,### |
| 20:4 n-6 | 13.7±2.4 | 13.9±1.0 | 13.8±1.1 | 15.1±1.4*,#,### |
| 20:5 n-3 | 0.2±0.1 | 0.2±0.1 | 0.2±0.1 | 0.2±0.1 |
| 22:4 n-6 | 0.4±0.1 | 0.5±0.2 | 0.7±0.1* | 0.7±0.2**,## |
| 22:5 n-3 | 0.4±0.2 | 0.4±0.1 | 0.5±0.2 | 0.3±0.1 |
| 22:6 n-3 | 2.4±0.5 | 2.4±0.4 | 2.5±0.5 | 1.7±0.3*,#,### |
| SFA | 48.2±3.6 | 44.6±1.2** | 44.5±1.7** | 44.6±1.8** |
| MUFA | 13.3±1.4 | 13.7±1.3 | 14.1±1.2 | 14.2±1.5 |
| Σ n-6 | 35.5±4.1 | 39.3±1.4* | 39.1±2.7* | 39.2±1.9* |
| Σ n-3 | 3.0±1.0 | 3.0±0.5 | 2.9±0.7 | 2.2±0.5*,#,### |
| PUFA | 38.6±4.7 | 42.3±1.3 | 42.1±3.0 | 41.8±2.1 |
| n-6/n-3 | 12.6±3.4 | 13.4±2.8 | 13.9±3.4 | 18.4±5.1*#,### |
| SFA/UNSFA | 1.0±0.2 | 0.8±0.1 | 0.8±0.1 | 0.8±0.1 |
| SFA/PUFA | 1.3±0.3 | 1.1±0.1** | 1.1±0.1** | 1.1±0.1** |
| 20:4/20:3 (Δ5) | 5.8±2.3 | 4.1±1.1* | 3.9±0.7** | 3.4±0.7*** |
| 20:3/18:2 (Δ6) | 0.1±0.1 | 0.2±0.0 | 0.2±0.0 | 0.2±0.1***,## |
| 22:6/22:5 (Δ4) | 6.0±1.4 | 5.6±0.7 | 5.4±2.6 | 5.1±0.9 |
| 18:1/18:0 (Δ9) | 0.8±0.1 | 0.9±0.1 | 1.0±0.1 | 1.1±0.2*,# |
| 18:0/16:0 (elongase) | 0.5±0.1 | 0.5±0.1 | 0.5±0.3 | 0.4±0.1 |

*$p$<0.05; **$p$<0.01; ***$p$< 0.001 when compared with CS I; #$p$<0.05; ##$p$<0.01 when compared with CS II, ###$p$< 0.05 when compared with CS III

There are not many data about activity of desaturase system in cancer. We estimated desaturase and elongase activity according to the specific FA ratios and we found significantly increased Δ6 and Δ9 desaturase activities in NHL patients, particularly in CS IV. High levels of SFA increase Δ9 desaturase activity by twofold to threefold, whereas PUFAs decrease it [41]. Thus, elevated percentages of 16:0 and 18:1, and lower 18:0 might reflect active desaturation from 18:0 to 18:1 [42]. Higher activity of Δ9 desaturase has already been reported in pancreatic and breast cancer patients [13, 41], and elevated Δ6 desaturase in oesophageal cancer and in children acute lymphoblastic leukemia [13, 43]. However, estimated activity of Δ5 desaturase in our NHL patients was reduced, while van Leeuwen et al. found higher activity of Δ5 desaturase in pancreatic and oesophageal cancer patients than in healthy subjects [13]. No abnormalities in desaturase function were reported in lung cancer [13] and acute myeloblastic leukemia [43], suggesting that type of cancer could be responsible for alterations in activity of desaturase systems. However, the possible effect of impaired absorption or impaired metabolism in the patient group on the level of particular FA and consequently estimated desaturase activity, could not be excluded.

This is the first study reporting FA profile and estimated desaturase activities in serum phospholipids in NHL patients. We showed significant differences compared with healthy population and most of our findings are supported by the literature data in other cancer types. Even though further studies on a larger number of patients are needed to establish the possible clinical role of measurement of FA profiles in patients with NHL, particularly in terms of supplementation, our results suggest the importance of nutritional intervention at an early stage of diagnosis, in order to limit nutrient depletion rather than attempting to treat the catabolic response at advanced stages.

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**Conflict of interest statement** There are no conflicts of interest related to this work.

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