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Sex-dependent association between omega-3 index and body weight status in older Australians

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ABSTRACT

Background/objectives: Restricting energy intake for weight management in older adults has potential to adversely affect nutritional status and result in impairment of an already compromised immune system. Investigation of alternative strategies to combat adiposity and sustain lean muscle mass in older adults are warranted to minimise the risk of developing chronic diseases. Long chain omega-3 polyunsaturated fatty acids (LCn-3PUFA), including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), may play an important role through their impact on increased fat oxidation and reduced inflammation. This study aimed to examine the association between erythrocyte membrane LCn-3PUFA and anthropometric measures in an older population.

Subjects/methods: A cross-sectional sample of older adults (n = 620; age 65–95 years; 56.3% females) from the Retirement Health and Lifestyle Study (RHLS) was analysed. Anthropometric measurements, including height, weight, body mass index (BMI), waist (WC) and hip circumference (HC) were taken. The fatty acid composition of erythrocyte membranes was analysed via gas chromatography (GC) to determine the omega-3 index (%EPA plus %DHA).

Results: An inverse association was detected between the omega-3 index and anthropometric measures, BMI ($r = -0.076$, $p=0.06$), WC ($r = -0.118$, $p < 0.01$) and waist-to-hip ratio (WHR; $r = -0.149$, $p < 0.001$). Stratification of data by sex (females, n = 349; males, n = 271) indicated that these associations were sex-specific. Females displayed an inverse association between the omega-3 index and BMI ($r = -0.146$, $p < 0.01$) and WC ($r = -0.125$, $p < 0.05$). In contrast, no significant association between the omega-3 index and anthropometric measures was detected in males. After correcting for the potentially confounding effects of age, household income, fish oil supplement status, daily dietary energy intake and total physical activity times, the omega-3 index was inversely associated with BMI and WC in females but not males.

Conclusions: Omega-3 status was associated with weight status, particularly in older women but not in men. These results suggest the need for sex-based intervention trials to examine the role of dietary intake and/or supplementation of LCn-3PUFA in weight management of older adults.

1. Introduction

Increasing prevalence of overweight and obesity in older adults heightens the risk of developing and/or aggravating non-communicable illnesses, such as type 2 diabetes (T2D) and cardiovascular disease (CVD) [1,2]. In 2011–12, 72% of Australian adults aged 65 years or older were overweight or obese and within the 65–74 years age group, over one in three were obese (35.2%) compared with approximately one in four in 1995 (24.8%) [3,4]. The proportion of older adults in Australia is projected to increase from 14% in 2012 to 19% in 2031 and 24% in 2061, and obesity will likely continue to be a major cause of morbidity and mortality [5].

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Current weight management strategies include lifestyle interventions, such as increases in physical activity and dietary restrictions, and pharmaceutical drug therapy for the morbidly obese. Excess body fat can limit the ability of older adults to participate in physical activity, and the long-term use of drugs for long-term maintenance of weight loss poses potential health risks [6–8]. Diet-induced weight loss can be readily achieved in the short-term but only a small proportion can sustain weight loss in the long-term [9,10]. Excess body fat is associated with the accumulation of fat in adipose tissue as well as elevated levels of pro-inflammatory mediators which increase the risk of obesity associated inflammatory diseases [8,11,12]. However, excessive weight is preventable, and therefore safe and efficacious intervention strategies are warranted to combat obesity and related health issues in older adults.

Long chain omega-3 polyunsaturated fatty acids (LCn-3PUFA), specifically eicosapentaenoic acid (EPA; 20:5n-3) and docosahexaenoic acid (DHA; 22:6n-3), have the potential to play an important role in ameliorating metabolic dysfunction, assisting weight control and reducing the risk of inflammatory disease in older adults [11]. The mechanisms explored in the literature include: (1) increased fat oxidation and increased thermogenesis, both of which lead to a decrease in fat deposition in adipose tissue [13]; (2) greater satiety and suppression of appetite following a LCn-3PUFA rich diet [14,15]; (3) altered expression of genes involved in regulating lipid metabolism [13,14,16]; (4) increases in adiponectin (a hormone synthesised by adipocytes involved in regulating lipid metabolism) [17]; and (5) facilitation of the synthesis of anti-inflammatory eicosanoids (signalling molecules) and inflammation resolving resolvins and protectins (lipid mediators) [11,12,18].

Several animal intervention trials have suggested a role of LCn-3PUFA in changes to weight status [14,16,19,20] but human studies have generated conflicting results. Most recently, two observational studies have reported an inverse association between erythrocyte levels of LCn-3PUFA and body weight status measures [21,22]. Randomised controlled trials have been less convincing, potentially due to small sample size, the relatively short duration of trials, varying assessment measures of LCn-3PUFA, and differences in subject criteria and fish oil supplementation dosage [23–26].

The omega-3 index reflects long-term (over several months), habitual dietary intake of LCn-3PUFA [27–29]. Therefore, the omega-3 index is a valid biomarker and measurement tool for determination of LCn-3PUFA status [22].

The aim of the current study was to examine, for the first time in older adults aged 65 years and over, whether there is an association between the omega-3 index and measures of body weight status including body mass index (BMI), waist circumference (WC) and waist-to-hip ratio (WHR).

2. Subjects and methods

2.1. Subjects and study design

This cross-sectional, observational study included male and female adults aged 65 years or older from the Retirement Health and Lifestyle Study (RHLS), a large cross-sectional study of the health and lifestyle of older adults living on the Central Coast of New South Wales (NSW), Australia. Participants were eligible for the RHLS if they: were ≥65 years of age; their primary residence was located within the Wyong or Gosford Local Government Areas; and they had been living at their current address for ≥12 months. Participants were not eligible if: they were not living independently or were residing in a communal setting other than a retirement village; another member of their household was taking part in the study; they had language and/or other communicative difficulties that limited participation; or they were cognitively impaired and/or were unable to provide informed consent. Eligible participants took part in an interviewer-administered questionnaire that collected information relating to subject demographics, medical history, medications and supplement data, physical activity levels, smoking status and alcohol consumption. In addition, participants completed self-administered paper-based questionnaires (food frequency and additional medical history) and attended a clinic where fasting blood samples and anthropometric measures were taken. Participants were included in the present study if they had erythrocyte samples for the determination of membrane fatty acid composition.

Written informed consent was obtained from all participants and the study was approved by the Human Research Ethics Committee of the University of Newcastle (Reference No. H-2008-0431) and the Northern Sydney Central Coast Health Human Research Ethics Committee (Reference No. 1001-031M).

2.2. Biochemical analyses

Fasted (≥10 h) blood samples were collected by a trained phlebotomist in accordance with protocol. Blood samples were centrifuged at 3000 × g for 10 min to separate plasma from erythrocyte fractions. The fatty acid composition of the erythrocyte cell membranes were determined via direct trans-esterification of the washed erythrocyte fraction followed by standardised gas chromatographic analyses (GC) [30,31]. A known fatty acid mixture was used to compare with analysed samples to identify peaks according to retention time and their concentration was determined using a Hewlett Packard 6890 Series GC with Chemstations Version A. 04.02 software. The omega-3 index was determined by summing erythrocyte membrane EPA and DHA expressed as a percentage of total erythrocyte fatty acids (%EPA plus %DHA).

2.3. Anthropometric measurements

Anthropometric measurements including height, weight, WC and hip circumference (HC), were taken by research project officers according to World Health Organisation (WHO) recommendations [32]. Weight was measured using calibrated standardised portable digital scales (Tanita HD-316, Tanita Corporation, Tokyo, Japan; or Wedderburn UWPM150, Wedderburn Scales, Australia). Two weight measurements were taken to the nearest 100 g to calculate a mean weight. Height was measured using a portable stadiometer (design no. 1013522, Surgical and Medical Products, Australia). Two height measurements were taken to the nearest 0.1 cm to calculate a mean height. For both weight and height measurements, participants were required to remove shoes and any heavy items of clothing or heavy objects from pockets. Mean weight and height were used to calculate BMI (non-obese< 0 kg/m^2, obese≥30 kg/m^2). WC and HC were measured using a stretch resistant, flexible tape. Two measurements were taken to the nearest 0.1 cm to calculate the mean values. WC was measured at the midway point between the lowest rib and iliac crest; HC was taken at the greatest posterior protuberance of the buttocks. Mean WC and HC were used to determine a WHR. For all anthropometric measures, if the two measurements varied more than the set tolerances of 800 g for weight, 1 cm for height, and 2 cm for WC and HC measurements were repeated until two measurements were within protocol. Health risk categories for both WC and WHR are based on current Australian guidelines [7,33,34]. In relation to WC, the guidelines indicate that adults are at increased disease risk if WC≥94 cm (for males) or WC≥80 cm (for females), or at greatly increased risk if WC≥102 cm (for males) or WC≥88 cm (for females) [7,34]. For WHR, adults are at increased disease risk if WHR>0.9 (for males) and WHR>0.8 (for females) [33,34].

2.4. Physical activity assessment

Physical activity was assessed via a series of questions that were adapted from validated questionnaires; the Active Australia Survey [35], RESIDE's Neighbourhood Physical Activity Questionnaire [36], the International Physical Activity Questionnaire [37], and the AusDiab General Questionnaire 04/05 [38]. Questions assessed levels of physical activity in the week prior to study participation. The frequency and duration of walking, moderate physical activity and vigorous physical activity were assessed. Total activity time was calculated by summing the time spent walking continuously for durations of 10 min or more with the time spent in moderate activity and twice the time spent in vigorous activity (not including gardening and yard work) [35].

2.5. Dietary intake and fish oil supplementation assessment

A self-administered food frequency questionnaire (FFQ) was adapted from the validated Commonwealth Scientific and Industrial Research Organisation (CSIRO) FFQ [39] and included 41 questions regarding usual dietary intake. Dietary intake data were analysed using Foodworks®Professional Edition 2009 Version 6.0.2562 (Xyris Software, Brisbane, Queensland, Australia) [40].

2.6. Statistical analysis

Study data were analysed using Statistical Package for the Social Sciences (SPSS; Release 22.0, Chicago, IL: SPSS Inc.). Data distributions were evaluated for normality, linearity and homoscedascity. Erythrocyte membrane fatty acid data were arcsine transformed and total activity time data was log transformed before analyses. Data are reported as the mean ± standard deviation (SD) or frequencies and percentage, as appropriate. Groups were compared using two-tailed chi-square analyses, independent sample t-tests and one-way ANOVA. Standard multiple regression analyses were used to assess the multivariate relationships between the omega-3 index and body weight status measures (BMI, WC and WHR) after correcting for the potentially confounding effects of age, household income, fish oil supplement status, daily energy intake and total activity time. Pearson product–moment correlation analyses were used to assess the bivariate relationships between variables. Separate correlation analyses were performed for male and female participants. Male and female participants were categorised into omega-3 index quartiles according to sex-specific omega-3 index quartile cut-offs. Differences in mean BMI, WC and WHR across omega-3 index quartiles were assessed using one-way ANOVA. Probability values of <0.05 were considered statistically significant.

3. Results

3.1. Participant characteristics

Participant characteristics for age, socio-demographic, fish oil supplement and hormone replacement therapy (HRT) use and physical activity levels are presented in Table 1 for the whole group and for male and female subgroups. The study population included 620 participants (females 56.3%) aged 65–95 years (mean 77.6 ± 6.9 years). There was no significant difference in mean age between males and females. Six hundred and five participants (267 males, 338 females) provided an estimate of their household income. Over ninety percent of participants reported household incomes of between $10,000 and $60,000, with the majority of these reporting household incomes between $10,000 and $40,000 (Table 1). Gender differences in the proportion of participants within each income bracket were found with a significantly higher proportion of females reporting household incomes of between $10,000 to $20,000, and a significantly lower proportion of females reporting household incomes of between $20,000 and $40,000, when compared to males (Table 1).

One hundred and sixty nine study participants reported taking fish oil supplements (62 males, 107 females; Table 1). Three hundred and seven female participants provided information regarding HRT use. Of these, 59.0% reported no history of HRT use, 12.4% reported they were currently using HRT and 28.7% reported taking HRT previously.

Study participants reported spending an average of 190.4 min in physical activity over the seven days prior to study participation, with the total time spent ranging from 0 to 1620 min (Table 1). The mean total activity time differed between males and females, with males reporting significantly higher total activity times than females. Male participants also reported a significantly higher mean daily energy intake when compared to female participants (Table 1).

Participant anthropometric characteristics for the whole group and the gender subgroups are presented in Table 2. The mean weight and height of male participants was significantly higher than female participants; however BMI was not significantly different between the two groups. According to BMI, 2.6% of the whole group were morbidly obese (BMI$\geq$40 kg/m^2), 31.9% were obese (BMI$\geq$30 kg/m^2), 42.7% were overweight (BMI 25–29.9 kg/m^2), 22.1% were healthy weight (BMI 18.5–24.9 kg/m^2) and 0.7% were underweight (BMI$<$18.5 kg/m^2). There was no significant difference in the proportion of males and females within each BMI category (Table 2).

The WC and WHR of male participants were significantly higher than female participants while the HC was not significantly different (Table 2). Based on current Australian guidelines to identify disease risk using abdominal adiposity measurements (WC and WHR), at least 82.8% of participants were either at increased risk or greatly increased risk of disease [7,34].

3.2. Erythrocyte fatty acids

Erythrocyte membrane fatty acid profiles were significantly different for male and female participants for total monounsaturated fatty acids (MUFA) and total polyunsaturated fatty acids (PUFA) but not total saturated fatty acids (SFA) (Table 3). Total erythrocyte membrane omega-6 PUFA was significantly lower in female participants compared with male participants but the reverse was true for total MUFA and total omega-3 PUFA, which were both significantly higher in female participants compared with male participants (Table 3).

With regards to LCn-3PUFA, mean erythrocyte docosapentaenoic acid (DPA; 22:5n-3) did not differ between male and females; however females had significantly higher EPA and DHA, and consequently higher omega-3 index scores, than male participants (Table 3).

When male and females groups were stratified as obese or non-obese, based on BMI, the omega-3 index of non-obese female participants was significantly higher than that of obese female participants ($p < 0.05$) (Fig. 1). There was no significant difference in omega-3 index between non-obese and obese male participants.

The results of bivariate correlation analyses of the relationships between erythrocyte omega-3 PUFA and anthropometric measures are presented in Table 4. When all participants were included in the analyses an inverse association between the omega-3 index and anthropometric measures, BMI ($r = -0.076$, $p = 0.06$), WC ($r = -0.118$, $p < 0.01$) and WHR ($r = -0.149$, $p < 0.001$) was observed. However, stratification of participants on sex indicated that these associations were gender specific (Table 4).

Table 1
Age, socio-demographic, fish oil supplement and hormone replacement therapy use and physical activity characteristics of study participants[b].

	Whole group	Males	Females	*p*-value
Number of subjects	620	271 (43.7)	349 (56.3)	
Age (years), mean ± SD	77.6 ± 6.9	77.3 ± 6.7	78.0 ± 7.1	ns
Annual household income				
Less than $10,000	4 (0.7)	0 (0.0)	4 (1.2)	
$10,000 to $20,000	201 (33.2)	44 (16.5)	157 (46.4)	
$20,000 to $40,000	292 (48.3)	159 (59.6)	133 (39.3)	
$40,000 to $60,000	66 (10.9)	39 (14.6)	27 (8.0)	
$60,000 to $80,000	23 (3.8)	15 (5.6)	8 (2.4)	
$80,000 to $100,000	13 (2.1)	7 (2.6)	6 (1.8)	
$100,000 or more	6 (1.0)	3 (1.1)	3 (0.9)	<0.001
Fish oil supplement use				
Non-supplemented	451 (72.7)	209 (77.1)	242 (69.3)	
Supplemented	169 (27.3)	62 (22.9)	107 (30.7)	<0.05
Hormone replacement therapy use				
No history	N/A	N/A	181 (59.0)	
Previous history	N/A	N/A	88 (28.7)	
Current	N/A	N/A	38 (12.4)	
Dietary energy intake				
Daily energy (kJ), mean ± SD	8041 ± 3107	8451 ± 3035	7723 ± 3129	<0.01
Physical activity[a]				
Total activity (mins), mean ± SD	190.4 ± 255.5	255.2 ± 295.8	140.3 ± 206.2	<0.001

[a] Total activity time was calculated by summing the time spent walking continuously for durations of 10 min or more with the time spent in moderate activity and twice the time spent in vigorous activity (not including gardening and yard work) over the 7 days prior to study participation.
[b] Data presented as frequency counts (percentage) unless otherwise indicated. Frequency counts and sample means were compared across male and female sub-groups using two-tailed chi-square analyses and independent samples t tests, respectively. For a number of parameters, subject numbers were reduced due to missing data.

There was a significant inverse association between the omega-3 index and BMI ($r = -0.146$, $p < 0.01$) and WC ($r = -0.125$, $p < 0.05$) in females participants (Table 4). Analyses of the relationship between the omega-3 index component fatty acids, DHA and EPA, and the anthropometric variables indicated that these relationships primarily reflected female-specific inverse associations between DHA and body weight status. In females, DHA was inversely associated with BMI ($r = -0.157$, $p < 0.01$), WC ($r = -0.142$, $p < 0.01$) and WHR ($r = -0.143$, $p < 0.01$), however, no relationship was detected between EPA and BMI, WC or WHR. In contrast, there was no significant association between the omega-3 index, or DHA or EPA, and any of the anthropometric measures in the male subgroup (Table 4).

Multiple regression analyses were conducted to assess the association between omega-3 index and the anthropometric variables, BMI, WC and WHR after adjusting for the potentially confounding variables; age, household income, fish oil supplement status, daily dietary energy intake and total physical activity times. The multivariate relationships between omega-3 index and each anthropometric measure were assessed separately and the results are summarised in Table 5. When combined in a multivariate analysis, age, household income, supplement status, daily energy intake, total physical activity time and omega-3 index were able to significantly predict BMI and WC in both males and females, and WHR in females. However, consistent with the bivariate findings, gender specificity in the relationships between anthropometric variables and omega-3 index was observed, with omega-3 index displaying an independent association with BMI and WC in females (BMI: $\beta = -0.167$, $p < 0.01$; WC: $\beta = -0.144$, $p < 0.05$) but not males.

The mean (±SD) BMI, WC and WHR scores for males and females sub-grouped into quartiles on the basis of their omega-3 index scores are presented in Table 6, together with the results of one-way ANOVA of group differences. In males, no significant group differences, or trends in the magnitude of the quartile means, were evident for BMI, WC or WHR. Similarly, no significant group differences in mean BMI or WC were detected across the female omega-3 index quartiles subgroups. However, BMI did decrease with increasing omega-3 index quartiles ($p = 0.078$). Differences in mean WHR were also detected in females ($p < 0.05$) reflecting a significant reduction in the mean WHR of participants in quartile 4 when compared to those in quartile 2 ($p < 0.05$).

No significant association was detected between the omega-3 index and participant's household income or daily energy intake (data not reported). There was also no significant association between HRT use and the omega-3 index or any of the individual LCn-3PUFA (EPA, DPA and DHA). A positive association between omega-

Table 2
Anthropometric characteristics of study participants[b].

	Whole group (n = 620)	Males (n = 271)	Females (n = 349)	*p*-value
Anthropometric measures				
Weight (kg)	76.2 ± 15.4	83.5 ± 14.9	70.5 ± 13.2	<0.001
Height (m)	1.63 ± 0.09	1.71 ± 0.07	1.57 ± 0.06	<0.001
BMI (kg/m^2)[a]	28.6 ± 4.8	28.6 ± 4.5	28.6 ± 5.1	ns
Morbidly obese, n (%)	16 (2.6)	4 (1.5)	12 (3.5)	
Obese, n (%)	195 (31.9)	87 (32.6)	108 (31.4)	
Overweight, n (%)	261 (42.7)	125 (46.8)	136 (39.5)	
Health weight, n (%)	135 (22.1)	49 (18.4)	86 (25.0)	
Underweight, n (%)	4 (0.7)	2 (0.7)	2 (0.6)	ns
WC (cm)	98.8 ± 13.6	104.9 ± 12.5	94.0 ± 12.4	<0.001
HC (cm)	109.3 ± 10.5	108.6 ± 9.1	109.8 ± 11.3	ns
WHR	0.90 ± 0.08	0.96 ± 0.07	0.86 ± 0.06	<0.001

[a] BMI categories defined as: Obese, BMI≥30 kg/m^2; Overweight, BMI 25–29.9 kg/m^2; Healthy weight, BMI 18.5–24.9 kg/m^2; Underweight, BMI<18.5 kg/m^2.
[b] Data presented as mean ± SD unless otherwise indicated. Sample means and frequency counts were compared across male and female sub-groups using two-tailed independent samples t tests and chi-square analyses, respectively.

Table 3
Erythrocyte fatty acid composition (% wt/wt) of study participants[a].

	Whole group (n = 620)	Males (n = 271)	Females (n = 349)	*p*-value
Saturated fatty acids (SFA)				
C16:0	22.9 ± 1.3	22.9 ± 1.3	22.8 ± 1.2	ns
C18:0	18.4 ± 1.5	18.4 ± 1.5	18.6 ± 1.3	ns
C20:0	0.6 ± 0.4	0.6 ± 0.4	0.6 ± 0.1	<0.05
∑SFA	**41.9 ± 2.3**	**41.9 ± 2.3**	**42.0 ± 2.0**	**ns**
Monounsaturated fatty acids (MUFA)				
C16:1n-7	0.5 ± 0.3	0.5 ± 0.3	0.6 ± 0.3	<0.01
C18:1n-7	1.7 ± 0.4	1.7 ± 0.4	1.8 ± 0.4	ns
∑MUFA	**2.3 ± 0.5**	**2.3 ± 0.5**	**2.4 ± 0.6**	**<0.01**
Polyunsaturated fatty acids (PUFA)				
C18:2n-6	8.9 ± 1.5	8.9 ± 1.5	8.7 ± 1.5	ns
C18:3n-6	0.2 ± 0.2	0.2 ± 0.2	0.2 ± 0.2	ns
C20:2n-6	0.3 ± 0.3	0.3 ± 0.3	0.3 ± 0.1	<0.001
C20:3n-6	1.6 ± 1.2	1.6 ± 1.2	1.4 ± 1.1	<0.05
C20:4n-6	16.7 ± 2.5	16.7 ± 2.5	16.6 ± 2.5	ns
∑n-6 PUFA	**27.7 ± 2.6**	**27.7 ± 2.6**	**27.2 ± 2.7**	**<0.05**
C18:3n-3	0.3 ± 0.1	0.3 ± 0.1	0.3 ± 0.1	ns
C20:5n-3 (EPA)	1.5 ± 0.8	1.5 ± 0.8	1.9 ± 1.2	<0.001
C22:5n-3 (DPA)	3.6 ± 0.7	3.6 ± 0.7	3.6 ± 0.8	ns
C22:6n-3 (DHA)	6.5 ± 1.4	6.5 ± 1.4	6.9 ± 1.4	<0.001
∑n-3 PUFA	**11.9 ± 2.5**	**11.9 ± 2.5**	**12.6 ± 2.8**	**<0.001**
Omega-3 index	**8.0 ± 2.1**	**8.0 ± 2.1**	**8.8 ± 2.4**	**<0.001**
∑LCn-3 PUFA	**11.6 ± 2.5**	**11.6 ± 2.5**	**12.4 ± 2.9**	**<0.001**

[a] Data presented as mean ± SD. Sample means were compared across male and female sub-groups using two-tailed independent samples t tests of the arcsine transformed fatty acid data.

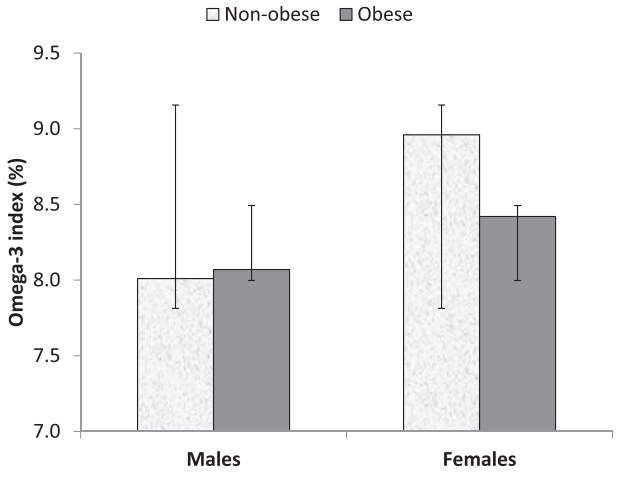

Fig. 1. Mean omega-3 index scores based on weight status in male and female sub-groups. The omega-3 index of non-obese (BMI < 30 kg/m^2) female participants (9.0% ± 2.5) was significantly higher than obese (BMI ≥ 30 kg/m^2) female participants (8.4% ± 2.2) ($p < 0.05$).

Table 4
Correlations between long chain omega-3 PUFA and anthropometric measurements[a].

	Whole group (n = 620)		Males (n = 271)		Females (n = 349)	
	r	*p*-value	r	*p*-value	r	*p*-value
EPA						
BMI	−0.077	ns	−0.026	ns	−0.105	ns
WC	−0.121	<0.01	−0.054	ns	−0.083	ns
WHR	−0.119	<0.01	−0.032	ns	−0.039	ns
DHA						
BMI	−0.064	ns	0.068	ns	−0.157	<0.01
WC	−0.100	<0.05	0.076	ns	−0.142	<0.01
WHR	−0.147	<0.001	0.032	ns	−0.143	<0.01
Omega-3 index						
BMI	−0.076	ns	0.037	ns	−0.146	<0.01
WC	−0.118	<0.01	0.031	ns	−0.125	<0.05
WHR	−0.149	<0.001	0.008	ns	−0.106	ns
∑LCn-3PUFA						
BMI	−0.097	<0.05	−0.009	ns	−0.152	<0.01
WC	−0.126	<0.01	−0.027	ns	−0.125	<0.05
WHR	−0.136	<0.001	−0.031	ns	−0.100	ns

[a] Data presented as Pearson's correlation coefficient (r). Bivariate correlation analyses were conducted using Pearson's product-moment correlation of the arcsine transformed n-3 PUFA data against the anthropometric measures.

3 index levels and total physical activity time was found (R = 0.091, p < 0.05). As expected, participants taking fish oil supplements had a higher omega-3 index (10.3 ± 2.1%) than non-supplemented participants (7.8 ± 1.9%, p < 0.001).

4. Discussion

This cross-sectional study suggests an inverse association between the omega-3 index and all anthropometric measures (BMI, WC and WHR) in older Australians. Stratification of the study cohort on gender highlighted that this association is only evident in females and not in males.

Relevant to this report is a unique set of characteristics that face the older adult population, including increased prevalence of obesity, an ageing demographic, the physiological and biological changes associated with ageing including compromised immunity, reduced lean muscle mass, reduced appetite and level of physical activity, and redistribution of fat towards visceral rather than subcutaneous adipose tissue [8,43]. The study highlighted that over one third (39.3%) of the participants aged 65–74 years were obese which is in line with the Australian Health Survey 2011–2012 that indicated that within the 65–74 year group 35.2% were obese [3]. In addition, based on abdominal adiposity measurements (WC and WHR), over 82% of participants were identified at increased health risk according to current Australian guidelines [7,34]. Abdominal obesity in older adults places them at increased risk of adverse metabolic consequences and susceptibility to co-morbidities including T2D, metabolic syndrome, CVD and arthritis [43].

While this is the first study to examine whether an association exists between LCn-3PUFA levels and body weight status in an

Table 5
Multiple regression analyses of the relationship between omega-3 index [41,42] and the anthropometric variables, BMI, waist circumference and waist to hip ratio after controlling for potential covariates[a].

	Males		Females	
BMI				
Model statistics	$R = 0.328$, $R^2 = 0.108$ $F(6,254) = 5.107$, $p < 0.001$		$R = 0.356$, $R^2 = 0.126$ $F(6,326) = 7.863$, $p < 0.001$	
Variables	β	*p*	β	*p*
Age	−0.211	<0.01	−0.217	<0.001
Household income	−0.040	ns	−0.171	<0.01
Fish oil supplement	−0.045	ns	0.099	ns
Daily energy intake	0.035	ns	0.003	ns
Total activity time	−0.258	<0.001	−0.215	<0.001
Omega-3 index	0.106	ns	−0.167	<0.01
Waist circumference				
Model statistics	$R = 0.326$, $R^2 = 0.106$ $F(6,255) = 5.060$, $p < 0.001$		$R = 0.307$, $R^2 = 0.094$ $F(6,329) = 5.704$, $p < 0.001$	
Variables	β	*p*	β	*p*
Age	−0.169	<0.01	−0.139	<0.05
Household income	−0.046	ns	−0.109	ns
Fish oil supplement	−0.025	ns	0.111	ns
Daily energy intake	0.018	ns	−0.022	ns
Total activity time	−0.288	<0.001	−0.226	<0.001
Omega-3 index	0.103	ns	−0.144	<0.05
Waist:Hip ratio				
Model statistics	$R = 0.217$, $R^2 = 0.047$ $F(6,254) = 2.099$, $p = 0.054$		$R = 0.205$, $R^2 = 0.042$ $F(6,327) = 2.398$, $p < 0.05$	
Variables	β	*p*	β	*p*
Age	−0.117	ns	0.031	ns
Household income	−0.090	ns	−0.065	ns
Fish oil supplement	−0.040	ns	0.069	ns
Daily energy intake	0.032	ns	−0.019	ns
Total activity time	−0.169	<0.01	−0.133	<0.05
Omega-3 index	0.070	ns	−0.114	ns

[a] Multiple regression analyses were conducted using the log transformed total physical activity data and arcsine transformed omega-3 index data. Total activity time (minutes) was calculated by summing the time spent walking continuously for durations of 10 min or more with the time spent in moderate activity and twice the time spent in vigorous activity (not including gardening and yard work) over the 7 days prior to study participation.

Table 6
Comparison of anthropometric characteristics for male and female participants across omega-3 index quartiles[a].

	Omega-3 index quartile				*p*-value
	1	2	3	4	
BMI (kg/m^2)					
Males	28.4 ± 4.7	27.9 ± 4.2	29.8 ± 4.6	28.5 ± 4.2	0.074
Females	29.4 ± 5.3	29.1 ± 5.1	28.3 ± 4.8	27.6 ± 5.0	0.078
WC (cm)					
Males	104.2 ± 13.5	102.9 ± 10.7	108.3 ± 13.5	104.3 ± 11.8	0.065
Females	95.1 ± 13.0	96.3 ± 12.6	92.7 ± 11.4	91.9 ± 12.0	0.061
WHR					
Males	0.97 ± 0.08	0.96 ± 0.06	0.97 ± 0.05	0.96 ± 0.06	0.980
Females	0.85 ± 0.06	0.87 ± 0.06	0.85 ± 0.06	0.84 ± 0.06	0.042

[a] Data presented as mean ± SD. p values are for the comparison of anthropometric variables across quartiles using one-way ANOVA. Participants were assigned into omega-3 index quartiles on the basis of their omega-3 index score separately for males and females. Increasing omega-3 index quartile numbers reflect increasing omega-3 index scores.

older adult population, previous observational studies have explored the possible association in adults, children and adolescents with consistent results in most cases [21,22,44–46]. Where conflicting results have been reported, variations in study design; sample size; study duration and the methodologies used to quantitate LCn-3PUFA, which have included investigation of dietary intake (using dietary food records and food frequency questionnaires) and analysis of plasma total lipids, plasma phospholipids or erythrocyte biomarkers, may have contributed.

Most recently in an observational study, Howe et al. [22] explored the association between erythrocyte levels of LCn-3PUFA and obesity in adults aged 34–60 years (n = 476). Consistent with the current findings, Howe et al. found an inverse association between erythrocyte LCn-3PUFA levels and adiposity (BMI, WC and body fat) that was evident in females but not males [22]. In addition, it was specifically DHA, and not EPA, that displayed the strongest association [22]. Harris et al. [21] analysed a larger cohort (n = 3196) from the Framingham Heart Study and reported an inverse association between erythrocyte LCn-3PUFA levels and WC, the sole body weight status measure included in that study [21]. Three smaller studies (n = 124 adults, n = 120 adolescents and n = 48 children) reported the same inverse association between erythrocyte or plasma LCn-3PUFA levels and varying anthropometric measures [44–46].

Conflicting results were reported in two large cohort studies that explored the relationship between dietary intake of LCn-3PUFA and overweight and obesity. The Health Professional Follow-up Study (n = 43,671 men) reported that dietary intake of LCn-3PUFA was associated with healthier weight status [47]. However, the Nurses' Health Study (n = 79,839 women) showed a positive association between higher intake of LCn-3PUFA and obesity prevalence [48]. While the possibility that gender differences could explain the contradictory results, both studies relied solely on FFQ data to estimate dietary intake of LCn-3PUFA.

Research indicates that fatty acid biomarkers (in plasma or erythrocyte membrane) are more accurate estimates of habitual dietary intake of fatty acids compared with questionnaire-based estimates and therefore are more reliable for assessment of associations with body weight status measures [22]. Of the two, erythrocyte fatty acids are considered to be the more superior marker as they reflect long-term dietary intake of fatty acids [27,29,49].

The gender differences in the current study support previous indications that fatty acid metabolism may be different in females compared with males due to the effects of sex hormones .[50, 51] _ENREF_48 Previous studies have indicated that conversion of α-linolenic (ALA) to DHA is mediated by the oestrogen hormone which enhances the capacity of females to synthesise DHA from ALA [52–55]. This may not be relevant to the current study as the female population group are post-menopausal and >65 years. However, female subjects may still have higher circulating oestrogen levels than male counterparts that influence levels of DHA and the omega-3 index; and there is some evidence to suggest that in females of post-menopausal age, HRT reduces the retroconversion of DHA to EPA [56]. However, in the current study we found no significant association between HRT use and levels of the LCn-3PUFA, including EPA and DHA. A recent study has shown that ingestion of ALA rich chia seeds resulted in significant increases in plasma EPA levels in post-menopausal women [57]. It is also possible that women have a lower capacity than men to retroconvert DHA to DPA and EPA [51]. Previous evidence does suggest that circulating LCn-3PUFA levels, and the omega-3 index, may not be solely determined by the amount of preformed EPA and/or DHA consumed in the diet, particularly for female participants [51]. Further investigation into the differences between male and female omega-3 index levels is beyond the scope of this report.

Several animal intervention trials have reported a reduction in body fat accumulation, particularly a reduction in visceral adipose tissue compared to subcutaneous adipose tissue, following high fat diets that included LCn-3PUFA [14,16,19,20]. These animal studies were all conducted in male rodents and therefore do not shed any

light on sex differences, but they do provide important findings relating to the potential effects of LCn-3PUFA on the deposition of fat in adipose tissue.

The human intervention trials that have explored the effects of increased intake of LCn-3PUFA on body weight status have generated conflicting results. The studies varied in sample size (n = 6 to 278), duration (6–24 weeks), subject characteristics (sex, age, health status), style of intervention, dietary-restriction regimes and doses of fish oil supplementation. Most recently, Harden et al. [23] conducted a double-blind, randomised, parallel intervention trial over 12 weeks and reported significantly lower energy intake, indicating the potential appetite suppressing effects of LCn-3PUFA. A fall in body weight approached statistical significance suggesting the need for a longer term study. Munro and Garg [25] conducted a double-blind randomised, placebo controlled intervention and demonstrated a greater percentage reduction in weight and BMI for females in the fish oil supplementation group compared to control.

In an earlier study, Thorsdottir et al. [26] explored the effects of fish consumption and fish oil supplementation as part of an energy-restricted diet in an overweight adult population. Greatest weight loss was evident in males who included fish or fish oil supplements, but not females. This study provides conflicting results surrounding gender differences but the short duration of the trial (eight weeks) limits the conclusions that can be drawn. Krebs et al. [24] also found similar results in an overweight, insulin-resistant female adult population (n = 93; aged 21–69 years) on a low fat/high carbohydrate weight-loss program with fish oil supplements. While this study provided no evidence of increased weight loss from inclusion of fish oil compared with placebo oil, it was recognised that the low fat/high carbohydrate diet could affect the provision of essential LCn-3PUFA from food sources, thereby potentially counteracting some benefit from fish oil supplementation [24].

It is recognised that body weight status is also affected by other lifestyle behaviours which could explain conflicting and/or the varying strength of associations in previous research. These could include the amount and intensity of physical activity, quality of diet and existing disease states. Physical activity for the older adult population, in the form of some aerobic plus resistance training, is beneficial for improving and/or maintaining physical function and muscle mass, and promotes independent living and quality of life [8]. The current study did not explore specific exercise activities of participants, but rather examined the total amount of time spent in physical activity.

Studies that examined increased intake of LCn-3PUFA with an exercise regime to assess effect on body weight status are limited and have conflicting results. Varying study design, outcome measures, participant baseline metabolic abnormalities and baseline fat mass may have contributed to this conflict. A more recent randomised control trial of the status of sedentary, overweight and obese adults over 24 weeks indicated no additional benefit of LCn-3PUFA supplementation, compared to a diet and exercise based weight loss program [58]. In contrast, Hill et al. [59] found reductions in body fat in a randomised control trial of overweight and obese adults with a combined intervention of LCn-3PUFA supplementation with a moderate-intensity exercise regime.

The small significant association in the current study does not indicate a causal relationship between LCn-3PUFA and body weight status but it does suggest the potential role of LCn-3PUFA to assist weight loss and/or weight gain when used in conjunction with appropriate dietary and physical activity strategies for the older adult population, particularly in women. Obesity is characterised as a condition with chronic low-grade inflammation and the anti-inflammatory properties of LCn-3PUFA are well recognised. The potential role of LCn-3PUFA to increase fatty acid oxidation to assist with weight control, ameliorate metabolic dysfunction and modulate inflammatory processes warrants further investigation.

The current study was strengthened by its large sample size of participants that were randomly selected and representative of the most recent trend of obesity among Australian older adults as reported in the Australian Health Survey [3]. The omega-3 index is a reliable, valid biomarker used to explore the relationship between LCn-3PUFA and body weight status and reflects intake over several months. While DPA is excluded from the determination of the omega-3 index, this study did consider DPA during analysis of the data (as part of *total* LCn-3PUFA); however there was very little difference in the association between anthropometric measures and total LCn-3PUFA versus the omega-3 index (data not reported).

The limitations of the current study include a lack of body composition data to compliment body weight status measures. The cross-sectional study design used data collected by the RHLS which included varying levels of fish oil supplementation and physical activity. It is acknowledged that the correlation coefficients are small, and that while statistically significant, the relationship between LCn-3PUFA and the anthropometrics characteristics may not be sufficient to contribute significantly to weight control in a clinical setting when used in isolation. However, research investigating the interactive effects of high dietary or supplemental intakes of LCn-3PUFA on weight reduction when used in isolation or in association with other weight loss methods in older populations is limited. The current study has identified an association between LCn-3PUFA and body weight status in elderly participants and indicates the need for further research regarding the clinical significance of these findings in assisting weight reduction in this age group.

In conclusion, the results indicate that omega-3 index was inversely associated with weight status in females, but not males. Mainstream strategies for treatment of overweight and obesity are not necessarily appropriate for this vulnerable population group and the results warrant future longer-term intervention trials to examine the role of increased intake of LCn-3PUFA via food sources and/or supplementation in weight management of older adults.

Author contributions

MG, MV and ML designed the research. EM, SN and KK were responsible for data collection. EM, SN and KK undertook the data analysis. EM, MG, SN, KK and AP drafted the manuscript. All authors read and approved the final version.

Conflict of interest

The authors declare no conflict of interest.

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References

[1] Australian Institute of Health and Welfare. Obesity Trends in Older

Australians. Canberra: AIHW; 2004.
[2] World Health Organization (WHO). Active Ageing: A Policy Framework. Geneva: WHO; 2002.
[3] Australian Bureau of Statistics (ABS). Australian Health Survey: Updated Results, 2011-2012. Canberra: ABS; 2013.
[4] Australian Bureau of Statistics (ABS). Profiles of Health, Australia. Canberra: ABS; 2013. p. 2011–3.
[5] Australian Bureau of Statistics (ABS). Population Projections, Australia, 2012 (Base) to 2101. Canberra: ABS; 2013.
[6] McLaughlin D, Adams J, Almeida OP, Brown W, Byles J, Dobson A, et al. Are the national guidelines for health behaviour appropriate for older Australians? Evidence from the men, women and ageing project. Australas. J. Ageing 2011;30:13–6.
[7] National Health and Medical Research Council (NHMRC). Clinical Practice Guidelines for the Management of Overweight and Obesity in Adults, Adolescents and Children in Australia. Melbourne: NHMRC; 2013.
[8] Villareal DT, Apovian CM, Kushner RF, Klein S. Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, the Obesity Society. Am. J. Clin. Nutr. 2005;82:923–34.
[9] Anderson JW, Konz EC, Frederich RC, Wood CL. Long-term weight-loss maintenance: a meta-analysis of US studies. Am. J. Clin. Nutr. 2001;74:579–84.
[10] Sumithran P, Prendergast LA, Delbridge E, Purcell K, Shulkes A, Kriketos A, et al. Long-term persistence of hormonal adaptations to weight loss. N. Eng. J. Med. 2011;365:1597–604.
[11] Calder PC. Mechanisms of action of (n−3) fatty acids. J. Nutr. 2012;142(3):592S–9S.
[12] Flachs P, Rossmeisl M, Bryhn M, Kopecky J. Cellular and molecular effects of n-3 polyunsaturated fatty acids on adipose tissue biology and metabolism. Clin. Sci. 2009;116:1–16.
[13] Buckley JD, Howe PRC. Anti-obesity effects of long-chain omega-3 polyunsaturated fatty acids. Obes. Rev. 2009;10:648–59.
[14] Perez-Matute P, Perez-Echarri N, Martinez JA, Marti A, Moreno-Aliaga MJ. Eicosapentaenoic acid actions on adiposity and insulin resistance in control and high-fat-fed rats: role of apoptosis, adiponectin and tumour necrosis factor-alpha. Br. J. Nutr. 2007;97:389–98.
[15] Parra D, Ramel A, Bandarra N, Kiely M, Martinez JA, Thorsdottir I. A diet rich in long chain omega-3 fatty acids modulates satiety in overweight and obese volunteers during weight loss. Appetite 2008;51(3):676–80.
[16] Ruzickova J, Rossmeisl M, Prazak T, Flachs P, Sponarova J, Veck M, et al. Omega-3 PUFA of marine origin limit diet-induced obesity in mice by reducing cellularity of adipose tissue. Lipids 2004;39(12):1177–85. PubMed PMID: 15736913.
[17] Gray B, Steyn F, Davies PSW, Vitetta L. Omega-3 fatty acids: a review of the effects on adiponectin and leptin and potential implications for obesity management. Eur. J. Clin. Nutr. 2013;67:1234–42.
[18] Titos E, Claria J. Omega-3-derived mediators counteract obesity induced adipose tissue inflammation. Prostagl. other Lipid Mediat. 2013:107.
[19] Baillee R, Takada R, Nakamura M, Clarke S. Coordinate induction of peroxisomal acyl-CoA oxidase and UCP-3 by dietary fishoil. Prostagl. Leukot Essent Fat. Acids 1999;60:351–6.
[20] Belzung F, Raclot T, Groscolas R. Fish oil n-3 fatty acids selectively limit the hypertrophy of abdominal fat depots in growing rats fed high-fat diets. Am. J. Physiol. 1993;264:R1111–8.
[21] Harris WS, Pottala JV, Lacey SM, Vasan RS, Larson MG, Robins SJ. Clinical correlates and heritability of erythrocyte eicosapentaenoic and docosahexaenoic acid content in the Framingham Heart Study. Atherosclerosis 2012;225:425–31.
[22] Howe PRC, Buckley JD, Murphy KJ, Pettman T, Milte C, Coates AM. Relationship between erythrocyte omega-3 content and obesity is gender dependent. Nutrients 2014;6:1850–60.
[23] Harden CJ, Dible VA, Russell JM, Garaiova I, Plummer SF, Barker ME, et al. Long-chain polyunsaturated fatty acid supplementation had no effect on body weight but reduced energy intake in overweight and obese women. Nutr. Res. 2014:17–24.
[24] Krebs JD, Browning LM, McLean NK, Rothwell JL, Mishra GD, Moore CS, et al. Additive benefits of long-chain n-3 polyunsaturated fatty acids and weight-loss in the management of cardiovascular disease risk in overweight hyperinsulinaemic women. Int. J. Obes. 2006;30:1535–44.
[25] Munro IA, Garg ML. Prior supplementation with long chain omega-3 polyunsaturated fatty acids promotes weight loss in obese adults: a double-blinded randomised controlled trial. Food Funct. 2013;4:650–8.
[26] Thorsdottir I, Tomasson H, Gunnarsdottir I, Gisladottir E, Kiely M, Parra MD, et al. Randomized trial of weight-loss-diets for young adults varying in fish and fish oil content. Int. J. Obes. 2007;31:1560–6.
[27] Brown A, Pang E, Roberts D. Persistent changes in the fatty acid composition of erythrocyte membranes after moderate intake of *n*-3 polyunsaturated fatty acids: study design implications. Am. J. Clin. Nutr. 1991;54:668–73.
[28] Harris WS, von Schacky C. The omega-3 index: a new risk factor for death from coronary heart disease. Prev. Med. 2004;39:212–20.
[29] Katan M, Deslypere J, van Birgelen A, Penders M, Zegwaard M. Kinetics of the incorporation of dietary fatty acids into serum cholesteryl esers, erythrocyte membranes, and adipose tissue: an 18-month controlled study. J. Lipid Res. 1997;38:2012–22.
[30] Lepage G, Roy CC. Direct transesterification of all classes of lipids in a one-step reaction. J. Lipid Res. 1986;27(1):114–20.
[31] Ferguson J, Veysey M, Lucock M, Niblett S, King K, MacDonald-Wicks L, et al. Association between omega-3 index and blood lipids in older Australians. J. Nutr. Biochem. 2015;27:233–40.
[32] Luepker RV, Evans A, McKeigue P, Srinath Reddy K. Cardiovascular Survey Methods. third ed. Geneva: World Health Organisation; 2004.
[33] Price GM, Uauy R, Breeze E, Bulpitt CJ, Fletcher AE. Weight, shape, and mortality risk in older persons: elevated waist-hip ratio, not high body mass index, is associated with a greater risk of death. Am. J. Clin. Nutr. 2006;84:449–60.
[34] Stewart R. Griffith Handbook of Clinical Nutrition and Dietetics. fourth ed. Brisbane: Australian Publishing; 2011.
[35] Australian Institute of Health and Welfare (AIHW). The Active Australia Survey: A Guide and Manual for Implementation, Analysis and Reporting. Canberra: AIHW; 2003.
[36] Giles-Corti B, Timperio A, Cutt H, Pikora TJ, Bull FC, Knuiman M, et al. Development of a reliable measure of walking within and outside the local neighbourhood: RESIDE's neighbourhood physical activity questionnaire. Prev. Med. 2006;42:455–9.
[37] Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity qustionnaire: 12 country reliability and validity. Med. Sci. Sports Exerc. 2003;35:1381–95.
[38] Dunstan DW, Zimmet PZ, Welborn TA, Cameron AJ, Shaw J, de Courten M, et al. The Australian Diabetes, Obesity and Lifestyle Study (AusDiab)—methods and response rates. Diabetes Res. Clin. Pract. 2002;57(2):119–29.
[39] Lassale C, Guilbert C, Keogh J, Syrette J, Lange K, Cox DN. Estimating food intakes in Australia: validation of the Commonwealth Scientific and Industrial Research Organisation (CSIRO) food frequency questionnaire against weighed dietary intakes. J. Hum. Nutr. Diet. 2009;22(6):559–66.
[40] Xyris Software (Australia) Pty Ltd. Foodworks Professional Edition 2009 Version 6.0.2562. Brisbane, QLD: Xyris Software; 2009.
[41] Harris WS. The omega-3 index as a risk factor for coronary heart disease. Am. J. Clin. Nutr. 2008;87:1997–2002.
[42] Schuchardt JP, Neubronner J, Block RC, Schacky C, Hahn A. Associations between Omega-3 Index increase and triacylglyceride decrease in subjects with hypertriglyceridemia in response to six month of EPA and DHA supplementation. Prostagl. Leukot. Essent. Fat. Acids 2014 Oct;91(4):129–34.
[43] DeCaria JE, Sharp C, Petrella RJ. Scoping review report: obesity in older adults. Int. J. Obes. 2012;36:1141–50.
[44] Burrows T, Collins CE, Garg ML. Omega-3 index, obesity and insulin resistance in children. Int. J. Pediatr. Obes. 2011;6:e532–9.
[45] Klein-Platat C, Drai J, Oujaa M, Schlienger JL, Simon C. Plasma fatty acid composition is associated with the metabolic syndrome and low-grade inflammation in overweight adolescents. Am. J. Clin. Nutr. 2005;82:1178–84.
[46] Micallef M, Munro I, Phang M, Garg ML. Plasma n-3 polyunsaturated fatty acids are negatively associated with obesity. Br. J. Nutr. 2009;102:1370–4.
[47] He K, Rimm EB, Merchant A. Fish consumption and risk of stroke in men. ACC Curr. J. Rev. 2003;12(2):43–4. 3//.
[48] Iso H, Rexrode K, Stampfer MJ. Intake of fish and omega-3 fatty acids and risk of stroke in women. ACC Curr. J. Rev. 2001;10(3):27. 5//.
[49] Harris WS. The omega-3 index: from biomarker to risk marker to risk factor. Curr. Atheroscler. Rep. 2009;11:411–7.
[50] Decsi T, Kennedy K. Sex-specific differences in essential fatty acid metabolism. Am. J. Clin. Nutr. 2011 Dec;94(Suppl. 6):1914S–9S.
[51] Crowe FL, Skeaff CM, Green TJ, Gray AR. Serum n-3 long-chain PUFA differ by sex and age in a population-based survey of New Zealand adolescents and adults. Br. J. Nutr. 2008;99:168–74.
[52] Burdge GC, Jones A, Wootton SA. Eicosapentaenoic and docosapentaenoic acids are the principal products of alphalinolenic acid metabolism in young men. Br. J. Nutr. 2002;88:355–63.
[53] Burdge GC, Wootton SA. Conversion of alphalinolenic acid to eicosapentaenoic, docosapentaenoic and docosahexaenoic acids in young women. Br. J. Nutr. 2002;88:411–20.
[54] Pawlosky R, Hibbeln J, Lin Y, Salem NJ. n-3 Fatty acid metabolism in women. Br. J. Nutr. 2003;90:993–4.
[55] Pawlosky RJ, Hibbeln JR, Lin Y, Goodson S, Riggs P, Sebring N, et al. Effects of beef- and fishbased diets on the kinetics of n-3 fatty acid metabolism in human subjects. Am. J. Clin. Nutr. 2003;77:565–72.
[56] Stark K, Holub B. Differential eicosapentaenoic acid elevations and altered cardiovascular disease risk factor responses after supplementation with docosahexaenoic acid in postmenopausal women receiving and not receiving hormone replacement therapy. Am. J. Clin. Nutr. 2004;79:765–73.
[57] Jin F, Nieman D, Sha W, Xie G, Qiu Y, Jia W. Supplementation of milled chia seeds increases plasma ALA and EPA in postmenopausal women. Plant Foods Hum. Nutr. 2012;67:105–10.
[58] DeFina LF, Marcoux LG, Devers SM, Cleaver JP, Willis BL. Effects of omega-3 supplementation in combination with diet and exercise on weight loss and body composition. Am. J. Clin. Nutr. 2011;93:455–62.
[59] Hill AM, Buckley JD, Murphy KJ, Howe PRC. Combining fish-oil supplements with regular aerobic exercise improves body composition and cardiovascular disease risk factors. Am. J. Clin. Nutr. 2007;85:1267–74.