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Effect of fatty and lean fish intake on lipoprotein subclasses in subjects with coronary heart disease: A controlled trial

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KEYWORDS:
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n-3 Fatty acids;
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BACKGROUND: Fish oil intake reduces serum triglycerides; however, little is known about the effects of dietary fish intake on lipoprotein subclasses.

OBJECTIVE: We aimed at assessing the effect of fatty and lean fish intake on the lipoprotein subclasses in an intervention study.

METHODS: The intervention study included 33 patients with coronary heart disease, who were aged 61.0 ± 5.8 (mean ± SD) years. The subjects were randomly assigned to a fatty fish (n = 11), lean fish (n = 12), or control (n = 10) diet for 8 weeks. Fish diets included at least 4 fish meals per week. Subjects in the control group consumed lean beef, pork, and chicken. Lipoprotein subclasses and their lipid components were determined by nuclear magnetic resonance spectroscopy.

RESULTS: Concentrations of n-3 fatty acids and docosahexaenoic acid increased in the fatty fish group. The concentrations of cholesterol, cholesterol esters, and total lipids in very large high-density lipoproteins (HDLs) increased in the fatty fish group (overall difference $P = .005$, $P = .002$, and $P = .007$, respectively; false discovery rate $P = .04$, $P = .04$, and $P = .05$, respectively). The mean size of HDL particles increased in the fatty fish group (9.8 ± 0.3 nm at baseline and 9.9 ± 0.4 nm at end of study; overall difference $P = .004$, false discovery rate $P = .04$). The fish diets did not affect very-low-density lipoprotein or low-density lipoprotein size.

CONCLUSION: Fatty fish intake at least 4 times per week increases HDL particle size which might have beneficial effect in patients with coronary heart disease.

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Fatty fish contains long-chain n-3 fatty acids, namely eicosapentaenoic and docosahexaenoic acids (EPA and DHA), which in several studies were shown to reduce serum triglycerides.[1,2] The effect of fish oils on total, low-density

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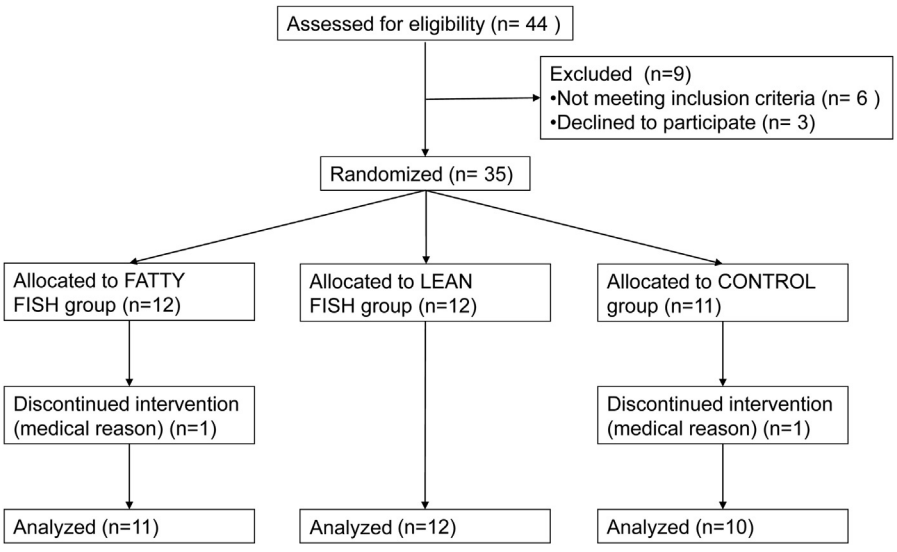

Figure 1 The subject flow.

lipoprotein (LDL), or high-density lipoprotein (HDL) cholesterol has been minor.[2] However, traditional lipid panels with total lipoprotein concentrations are inadequate to evaluate changes in multiple characteristics of the lipoproteins, such as those of HDL.[3,4] With the use of nuclear magnetic resonance (NMR) spectroscopy, lipoprotein particles of different sizes and a variety of lipid constituents in unfractionated serum and plasma can be analyzed.[5–7] Knowledge on the association between lipoprotein particles and cardiovascular disease (CVD) risk has deepened with the use of the new measures; for example, in some studies large HDL particles have been associated with lower CVD risk, whereas small HDL particles have been associated with higher CVD risk.[8,9] However, a recent study suggested that the average HDL diameter does not significantly differ between young patients with myocardial infarction and controls.[10]

Only few dietary interventions have reported results on lipoprotein subclass profiles.[11,12] Some studies that assessed the effect of use of fish oil or DHA oil supplements have been published.[13–16] Only 1 study has previously assessed the effect of fish within the context of low saturated-fat diet on lipoprotein particles.[11] We have

Table 1 Characteristics of the subjects at baseline of the intervention

	Fatty fish (n = 11)	Lean fish (n = 12)	Control (n = 10)	*P* value*
Age, years, mean ± SD	62.1 ± 6.3	60.7 ± 5.1	60.2 ± 6.4	.58
Sex, female/male, n/n	3/8	2/10	1/9	.75
Body mass index (calculated as kg/m^2), mean ± SD	26.8 ± 3.1	27.8 ± 2.1	27.0 ± 2.8	.63
Systolic blood pressure, mm Hg, mean ± SD	124 ± 16	126 ± 11	129 ± 14	.69
Diastolic blood pressure, mm Hg, mean ± SD	81 ± 8	84 ± 9	82 ± 9	.70
Current smoking, n	1	1	2	.71
Use of medications, n				
Use of statin†				.34
Atorvastatin	4	7	3	
Simvastatin	5	5	4	
Rosuvastatin	2	0	3	
Aspirin	10	11	8	.66
ACE inhibitor	3	6	6	.30
Calcium antagonist	3	4	2	.78
Oral anticoagulant	4	4	5	.71
Nitrate	2	4	3	.70

ACE, angiotensin-converting enzyme.
*Determined by analysis of variance or χ^2 test.
†The doses of statins were 10–40 mg/d for atorvastatin and simvastatin and 10–20 mg/d for rosuvastatin.

previously shown that during fatty fish intake there was a trend toward increase in total HDL cholesterol, whereas total and LDL cholesterol and triglycerides did not change.[17] The purpose of this study was to further explore the effect of fatty and lean fish intake on serum lipids by analyzing lipoprotein subclass profiles and serum lipid extracts by using NMR in patients with coronary heart disease (CHD).

Methods

Subjects

The intervention has been described in detail earlier.[17] Briefly, patients who had been in the Kuopio University Hospital because of acute myocardial infarction or unstable ischemic heart attack were asked to volunteer for the study. Thirty-five eligible subjects entered the study and were randomly assigned to a fatty fish, lean fish, or control diet (Fig. 1). Subjects gave written consent for participation in the study which was approved by the Research Ethics Committee of Hospital District of Northern Savo (registered in www.clinicaltrials.gov as NCT00720655).

Study design

The fish diets included at least 4 fish meals per week. The subjects in the fatty fish group were instructed to use salmon, rainbow trout, Baltic herring, whitefish, vendace, and tuna, whereas the subjects in the lean fish group used pike, pikeperch, perch, saithe, and cod. The control diet included lean beef, pork, or poultry and <1 portion of fish per week. Use of fish oil supplements was not allowed during the study or 3 months before the study. The intervention duration was 8 weeks, and 33 subjects completed the study. Subject's habitual dietary intake was estimated by a 4-day food record, and compliance was monitored with 7-day food records at weeks 3 and 7 (consecutive predefined days). Nutrient intake was calculated with the Micro-Nutrica dietary analysis program version 2.5 (Finnish Social Insurance Institute, Turku, Finland), which is based on Finnish analyses and international food composition tables.

Lipoprotein subclass and serum lipid analysis by NMR spectroscopy

Fasting serum samples taken at 0 and 8 weeks in the intervention study were used for the analysis of lipoprotein subclasses. Serum samples were frozen in −70°C until analyzed. The details of the methodology have been described previously,[5,18] and this platform has recently been applied in various large-scale epidemiologic and genetic studies.[19–22] The lipoprotein subclass data available were as follows: chylomicrons and largest very-low-density lipoprotein (VLDL) particles (average particle diameter, at least 75 nm); 5 different VLDL subclasses: very large VLDL (average particle diameter, 64.0 nm),

Table 2 Nutrient intake of the subjects at baseline and during the intervention

	Fatty fish (n = 11)		Lean fish (n = 12)		Control (n = 10)		
	Baseline*	During the study†	Baseline*	During the study†	Baseline*	During the study†	*P* value‡
Energy, kJ	6179 ± 1272	6586 ± 1150	7286 ± 1902	6738 ± 1803	8251 ± 3052	7273 ± 1785	.05
Fat, percentage of energy	30.9 ± 6.4	30.8 ± 5.3	30.9 ± 4.4	26.6 ± 3.6	30.7 ± 7.0	28.9 ± 4.9	.19
Saturated fat, percentage of energy	10.5 ± 3.7	9.4 ± 2.5	10.4 ± 3.4	8.0 ± 2.1	11.7 ± 3.3	10.1 ± 2.7	.54
Monounsaturated fat, percentage of energy	10.8 ± 2.7	10.4 ± 2.5	10.3 ± 1.3	9.1 ± 1.6	10.1 ± 2.4	9.8 ± 1.7	.60
Polyunsaturated fat, percentage of energy	5.7 ± 1.1	7.2 ± 1.1§	6.5 ± 1.4	6.4 ± 0.9	5.4 ± 2.3	5.6 ± 1.4	.04
Eicosapentaenoic + docosahexaenoic acids, g/d	0.44 ± 0.24	1.07 ± 0.41§	0.51 ± 0.71	0.44 ± 0.14	0.34 ± 0.36	0.16 ± 0.11	.003

Values are means ± SD.
*Calculated from 4-day food record.
†Mean intake calculated from 7-day food records at weeks 3 and 7.
‡Determined by general linear model for repeated measurements.
§$P \leq .05$ baseline vs during the study.

large VLDL (average particle diameter, 53.6 nm), medium VLDL (average particle diameter, 44.5 nm), small VLDL (average particle diameter, 36.8 nm), and very small VLDL (average particle diameter, 31.3 nm); intermediate-density lipoprotein (average particle diameter, 28.6 nm); 3 LDL subclasses: large LDL (average particle diameter, 25.5 nm), medium LDL (average particle diameter, 23.0 nm), and small LDL (average particle diameter, 18.7 nm); and 4 HDL subclasses: very large HDL (average particle diameter, 14.3 nm), large HDL (average particle diameter, 12.1 nm), medium HDL (average particle diameter, 10.9 nm), and small HDL (average particle diameter, 8.7 nm). The following components of the lipoprotein particles were quantified: phospholipids, triglycerides, cholesterol, free cholesterol, and cholesterol esters. Because of resolution and concentration issues all of these components are not available for every subclass.[18] The mean size for VLDL, LDL, and HDL particles was calculated by weighting the corresponding subclass diameters with their particle concentrations. Intermediate-density lipoprotein particles were included in the LDL measure.

After analyzing the serum lipoproteins, lipid extraction and the following NMR experimentation were performed as described earlier.[18]

Statistical analyses

Statistical analyses were performed with SPSS 19 (IBM SPSS Statistics, IBM Corp, Armonk, NY). The normality of the variables were tested with Shapiro-Wilk test, and for the variables not complying with the assumption logarithmic transformations were used in statistical testing. The effect of dietary intervention on lipoprotein subclass profile and serum lipid extracts was tested with general linear models for repeated measurements that adjusted for age and sex or Kruskall-Wallis test in case of skewed variables. Benjamini-Hochberg false discovery rate (FDR) was used to adjust results for multiple comparisons.[23] FDR-adjusted

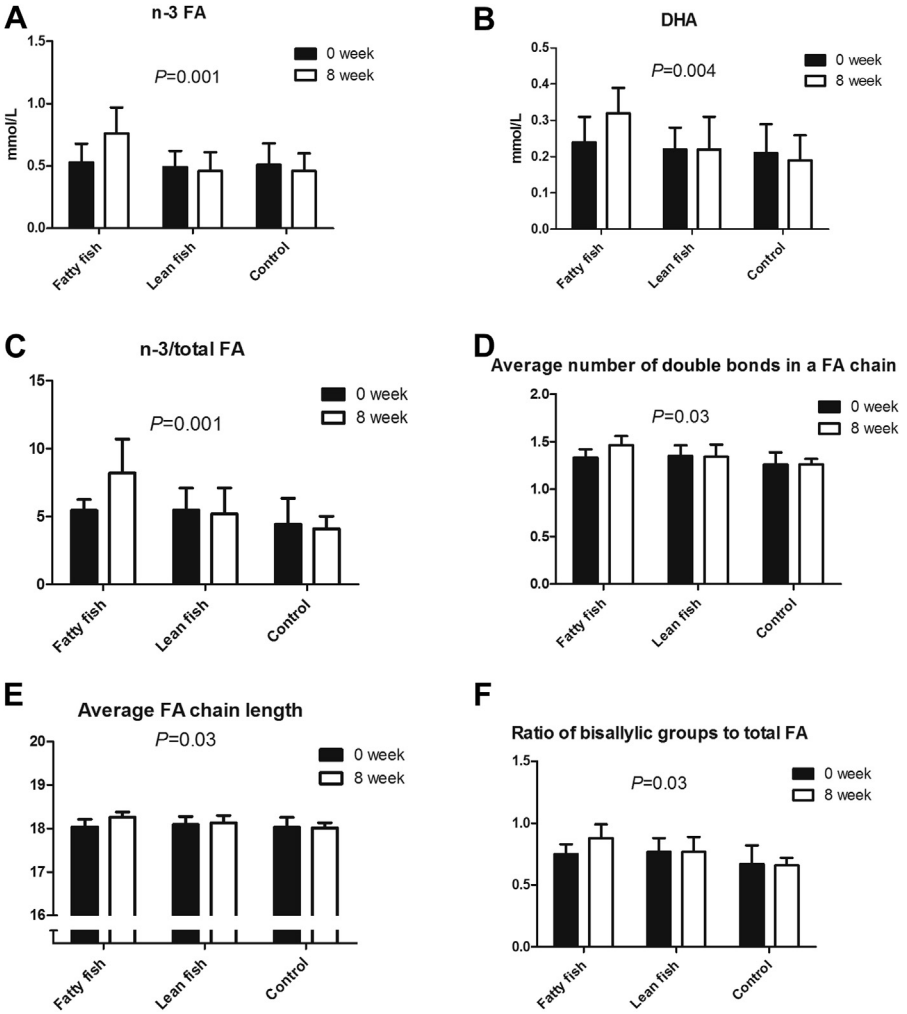

Figure 2 Serum lipid extracts, n-3 fatty acids (A), Docosahexaenoic acid (B), n-3/total fatty acids (C), Average number of double bonds in a fatty acid chain (D), Average fatty acid chain length (E), Ratio of bisallylic groups to total fatty acids (F) at baseline and after the intervention. Values are means ± SD. General linear model for repeated measurements was adjusted for sex and age; false discovery rate–corrected *P* values are shown. DHA, docosahexaenoic acid, FA, fatty acids.

$P \leq .05$ was considered as being statistically significant. In case of significant overall difference, the pairwise comparisons between the intervention groups were analyzed to compare the within-group changes of the variables by using analysis of variance, followed by multiple comparisons test with Bonferroni correction.

Results

The subjects in the intervention study were aged 61.0 ± 5.8 years (mean ± SD), and all of them were using statin and β-blocker medications (Table 1). No changes in lipid medication use was found during the study, except in the control group in which 1 subject stopped using atorvastatin and 1 subject stopped atorvastatin and started simvastatin. The types of statins did not differ among the groups. One subject in the fatty fish group and 1 subject in the lean fish group used ezetimibe. None of the subjects used fibrates or niacin.

The mean reported number of fish meals was 4.3 ± 0.4, 4.7 ± 1.1, and 0.6 ± 0.4 per week in the fatty fish, lean fish, and control groups, respectively, during the study. Accordingly, the intake of polyunsaturated fatty acids and EPA + DHA increased in the fatty fish group (Table 2). The intake of saturated and monounsaturated fat did not change significantly in the groups during the study.

As expected, concentrations of n-3 fatty acids and DHA increased in the fatty fish group (Fig. 2). Similarly, the ratio of n-3 fatty acids to total fatty acids increased in the fatty fish group. The average number of double bonds in fatty acid and average length of fatty acid chain increased in the fatty fish group. The ratio of bisallylic groups to total fatty acids increased in the fatty fish group.

Concentration of cholesterol in all HDL particles categories, and the size of HDL particles increased in the fatty fish group (overall difference $P = .003$ and $P = .004$, respectively, in general linear models and FDR-adjusted $P = .04$ for both) (Table 3). The mean particle size of VLDL or LDL did not change. Serum concentrations of cholesterol, cholesterol esters, and total lipids in very large HDL particles increased in the fatty fish group, whereas a decrease was found in the lean fish and control groups (overall differences $P = .005$, $P = .002$, and $P = .007$, respectively, and FDR $P = .04$, $P = .04$, and $P = .05$, respectively) (Table 4). The concentrations of VLDL and LDL subclass particles did not differ among the groups.

Discussion

We showed that fatty fish intake 4 times per week significantly increased HDL particle size in subjects with CHD in a controlled dietary intervention. These results are robust because the main differences across the groups were consistent and significant even after conservative statistics. We are aware of only 1 previous clinical trial that assessed the effect of fish intake on NMR lipid data that could indirectly support our finding that fatty fish intake beneficially affects HDL particle size. In that study, the National

Table 3 Major lipoprotein fractions and mean size of lipid particles at baseline (0 week) and after the intervention (8 weeks)

	Fatty fish (n = 11)		Lean fish (n = 12)		Control (n = 10)			FDR
	0 Week	8 Weeks	0 Week	8 Weeks	0 Week	8 Weeks	*P* value*	*P* value
Serum total cholesterol, mmol/L	3.90 ± 0.63	4.04 ± 0.52	3.75 ± 0.68	3.76 ± 0.46	4.50 ± 0.59	4.26 ± 0.64	.10	.27
Cholesterol in LDL, mmol/L	1.29 ± 0.30	1.31 ± 0.27	1.28 ± 0.39	1.32 ± 0.28	1.71 ± 0.28	1.55 ± 0.33	.19	.35
Cholesterol in HDL, mmol/L	1.46 ± 0.39	1.60 ± 0.37†,‡	1.36 ± 0.28	1.28 ± 0.27	1.41 ± 0.43	1.34 ± 0.33	.003	.04
Serum total triglycerides, mmol/L	1.12 ± 0.53	0.93 ± 0.40	1.03 ± 0.53	1.02 ± 0.42	1.63 ± 0.92	1.45 ± 0.37	.39	.47
Triglycerides in VLDL, mmol/L	0.77 ± 0.51	0.61 ± 0.35	0.68 ± 0.44	0.68 ± 0.37	1.16 ± 0.83	1.04 ± 0.34	.31	.40
Mean particle sizes, nm								
VLDL particles	36.5 ± 1.9	36.0 ± 1.4	36.3 ± 1.2	36.1 ± 1.3	37.6 ± 2.1	37.7 ± 1.4	.66	.70
LDL particles	23.5 ± 0.3	23.5 ± 0.2	23.5 ± 0.2	23.6 ± 0.2	23.3 ± 0.3	23.4 ± 0.2	.27	.40
HDL particles	9.8 ± 0.3	9.9 ± 0.4‡,§	9.8 ± 0.2	9.7 ± 0.2	9.7 ± 0.4	9.7 ± 0.3	.004	.04

FDR, false discovery rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very-low-density lipoprotein.
Values are means ± SD.
*Determined by general linear model for repeated measurements adjusted for sex and age.
†$P < .01$ for change in fatty fish vs change in control group (Bonferroni-corrected pairwise comparison).
‡$P < .01$ for change in fatty fish vs change in lean fish group (Bonferroni-corrected pairwise comparison).
§$P < .05$ for change in fatty fish vs change in control group (Bonferroni-corrected pairwise comparison).

Table 4 Lipoprotein subclass particle concentrations at baseline (0 week) and after the intervention (8 weeks)

	Fatty fish (n = 11)		Lean fish (n = 12)		Control (n = 10)			FDR
	0 Week	8 Weeks	0 Week	8 Weeks	0 Week	8 Weeks	*P* value*	*P* value
Chylomicrons and largest VLDL particles, nmol/L	0.05 ± 0.01	0.01 ± 0.02	0.05 ± 0.01	0.03 ± 0.06	0.01 ± 0.02	0.06 ± 0.08	.28†	.40
Very large VLDL, nmol/L	0.50 ± 0.69	0.28 ± 0.28	0.41 ± 0.65	0.33 ± 0.46	0.11 ± 1.34	0.84 ±.051	.85†	.88
Large VLDL, nmol/L	3.46 ± 3.65	2.14 ± 1.97	2.78 ± 3.29	2.51 ± 2.73	6.76 ± 6.66	5.69 ± 2.78	.48†	.53
Total lipids in large VLDL, mmol/L	0.22 ± 0.23	0.14 ± 0.12‡	0.19 ± 0.21	0.17 ± 0.16	0.42 ± 0.41	0.36 ± 0.17	.02†	.10
Medium VLDL, nmol/L	13.6 ± 9.5	10.8 ± 6.8	11.7 ± 8.2	11.9 ± 7.3	20.8 ± 14.8	19.3 ± 6.6	.30	.40
Small VLDL, nmol/L	26.3 ± 9.1	24.7 ± 8.8	24.9 ± 9.7	26.0 ± 7.7	34.7 ± 13.8	33.4 ± 7.2	.48	.53
Very small VLDL, nmol/L	28.9 ± 5.1	27.8 ± 7.2	28.5 ± 6.3	30.7 ± 4.1	31.2 ± 7.5	31.8 ± 7.1	.16	.35
IDL, nmol/L	66.3 ± 11.7	65.6 ± 13.7	66.6 ± 11.4	69.8 ± 9.7	75.9 ± 14.0	73.8 ± 15.0	.28	.40
Large LDL, nmol/L	112.6 ± 21.1	112.2 ± 20.3	111.6 ± 24.4	114.9 ± 19.4	138.9 ± 20.5	129.8 ± 23.3	.24	.40
Medium LDL, nmol/L	93.1 ± 22.4	92.7 ± 19.1	92.1 ± 25.0	93.2 ± 17.3	122.4 ± 20.3	111.0 ± 20.8	.29	.40
Small LDL, nmol/L	109 ± 30	109 ± 23	109 ± 35	106 ± 19	148 ± 28	129 ± 25	.26	.40
Very large HDL, nmol/L	303 ± 226	403 ± 233	284 ± 145	208 ± 127	303 ± 266	237 ± 173	.02	.10
Cholesterol in very large HDL (mmol/L)	0.21 ± 0.12	0.28 ± 0.11‡,§	0.21 ± 0.08	0.16 ± 0.06	0.25 ± 0.13	0.19 ± 0.08	.005	.04
Free cholesterol in very large HDL, mmol/L	0.05 ± 0.03	0.07 ± 0.03	0.05 ± 0.03	0.04 ± 0.02	0.05 ± 0.04	0.04 ± 0.03	.06	.21
Phospholipids in very large HDL, mmol/L	0.17 ± 0.14	0.22 ± 0.16	0.15 ± 0.10	0.11 ± 0.09	0.16 ± 0.17	0.12 ± 0.11	.35	.44
Cholesterol esters in very large HDL, mmol/L	0.16 ± 0.08	0.21 ± 0.07‡,§	0.16 ± 0.05	0.13 ± 0.04	0.19 ± 0.09	0.15 ± 0.06	.002	.04
Total lipids in very large HDL, mmol/L	0.39 ± 0.26	0.51 ± 0.26‡,§	0.37 ± 0.17	0.28 ± 0.14	0.41 ± 0.30	0.32 ± 0.19	.007	.05
Large HDL, nmol/L	851 ± 546	1034 ± 549	750 ± 348	672 ± 310	690 ± 631	653 ± 443	.18	.35
Cholesterol in large HDL, mmol/L	0.36 ± 0.23	0.46 ± 0.22	0.33 ± 0.16	0.28 ± 0.13	0.31 ± 0.27	0.29 ± 0.19	.06	.21
Free cholesterol in large HDL, mmol/L	0.07 ± 0.06	0.09 ± 0.06	0.06 ± 0.04	0.05 ± 0.03	0.06 ± 0.06	0.05 ± 0.05	.09	.27
Phospholipids in large HDL, mmol/L	0.31 ± 0.19	0.36 ± 0.19	0.28 ± 0.12	0.25 ± 0.11	0.25 ± 0.22	0.24 ± 0.15	.19	.35
Cholesterol esters in large HDL, mmol/L	0.30 ± 0.17	0.37 ± 0.17	0.27 ± 0.13	0.23 ± 0.10	0.26 ± 0.20	0.24 ± 0.15	.05	.21
Total lipids in large HDL, mmol/L	0.68 ± 0.43	0.84 ± 0.43	0.60 ± 0.28	0.53 ± 0.25	0.56 ± 0.50	0.52 ± 0.36	.10	.27
Medium HDL, nmol/L	1530 ± 286	1399 ± 307	1417 ± 202	1440 ± 210	1487 ± 313	1478 ± 230	.12	.30
Small HDL, nmol/L	4390 ± 410	4250 ± 450	4200 ± 260	4210 ± 240	4520 ± 400	4480 ± 360	.40	.47

FDR, false discovery rate; HDL, high-density lipoprotein; IDL, intermediate-density lipoprotein; LDL, low-density lipoprotein; VLDL, very-low-density lipoprotein.
Values are means ± SD.
*Determined by general linear model for repeated measurements adjusted for sex and age.
†*P* value for comparison of change (week 8 with week 0) among the groups was tested by Kruskall-Wallis test.
‡$P < .01$ for change in fatty fish vs change in control group (Bonferroni-corrected pairwise comparison).
§$P < .01$ for change in fatty fish vs change in lean fish group (Bonferroni-corrected pairwise comparison).

Cholesterol Education Program (NCEP) Step 2 diet with low intake of fish reduced HDL particle size, but NCEP Step 2 diet with high fish intake (consisting mostly of fatty fish) did not significantly affect HDL size compared with the average American diet.[11] Of note is that the average American diet provided more fat (35% of energy) than the NCEP Step 2 diets (approximately 26% of energy), which can also modify HDL concentration.

In other earlier trials, supplementation of fish oil or DHA oil has yielded higher amounts of n-3 fatty acids than what is typically derived from dietary fish intake. Concentration of large HDL particles increased after using fish oil (daily approximately 1.5 g of long-chain n-3 fatty acids)[24] or DHA oil (daily 2–3 g of DHA).[13,16] Mostad et al[14] reported reduced concentration of large VLDL and small HDL particles and a tendency toward larger HDL particle size after ingestion of fish oil that yielded daily 1.8 g of EPA and 3.0 g of DHA. In a cross-sectional setting, higher intake of n-3 fatty acids was associated with larger HDL size and smaller VLDL size in Alaska Natives.[25]

Anti-inflammatory effects are suggested to contribute to the beneficial effects of fatty fish.[1] The atheroprotective effect of HDL may be related to anti-inflammatory regulation, and a relation between inflammation and reverse cholesterol transport is suggested.[3] The phospholipid concentration of HDL is suggested to affect the anti-inflammatory properties of HDL.[26] The phospholipid concentration in very large HDL did not significantly change in the fatty fish group; however, we have previously reported decreases in ceramides, lysophosphatidylcholines, and diacylglycerols in the fatty fish group,[27] which may be related to anti-inflammatory effects.

Serum lipid extract analyses showed increases in DHA, n-3 fatty acids, and ratio of n-3 fatty acids to total fatty acids in the fatty fish group. The results are consistent with our earlier fatty acid analyses measured with gas chromatography.[17] With the use of similar metabolite quantification by NMR, higher DHA has been shown to be related to decreased risk for incident high intima-media thickness.[21] In addition to traditional fatty acid measurements with the use of gas chromatography, the lipid extract analyses showed changes in the average number of double bonds and chain length, which can be anticipated on the basis of the dietary intake of EPA (20:5) and DHA (22:6). The ratio of bisallylic groups to total fatty acids also increased in the fatty fish group, which can indicate increased proneness to oxidation.[28]

No significant effect on the concentration or size of LDL particles was observed after the fish diets, which is supported by an earlier study that showed no difference in LDL size between high-fish and low-fish NCEP Step 2 diets.[11] Fish protein has been suggested to have hypocholesterolemic effects in animal models,[29] whereas in humans the effect has not been repeated.[30] We did not observe significant differences in the response of lipoprotein particles to the lean fish diet compared with the control diet that included lean beef, pork, and chicken.

Small sample size is a limitation of our study. However, the number of subjects in the intervention study is comparable with some earlier studies.[11,14] The duration of the study was 8 weeks. Further study will be needed to determine the long-term effect of fish intake on lipoprotein particles and the effects in other populations. The subjects in the intervention study were using multiple medications as part of their regular CHD treatment, and all of them used statins and β-blockers. Possible confounding of the associations due to medications cannot be excluded because statins have been shown to increase HDL particle size.[31] In our study, however, the compositional changes in HDL and particle size were independent of statin use. Similarly, it has been reported earlier that lipoprotein particle changes caused by lifestyle intervention were independent of lipid-lowering medication use.[32]

Conclusion

Our results suggest that consumption of fatty fish at least 4 times per week has beneficial effects on HDL particle size. HDL modification might be related to its anti-inflammatory properties.

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