Effect of Dietary Counseling on a Comprehensive Metabolic Profile from Childhood to Adulthood

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Objectives To study the effects of repeated, infancy-onset dietary counseling on a detailed metabolic profile. Effects of dietary saturated fat replacement on circulating concentrations of metabolic biomarkers still remain unknown.

Study design The Special Turku Coronary Risk Factor Intervention Project (STRIP) study is a longitudinal, randomized atherosclerosis prevention trial in which repeated dietary counseling aimed at reducing the proportion of saturated fat intake. Nuclear magnetic resonance metabolomics quantified circulating metabolites from serum samples assessed at age 9 (n = 554), 11 (n = 553), 13 (n = 508), 15 (n = 517), 17 (n = 457), and 19 (n = 417) years.

Results The intervention reduced dietary intake of saturated fat (mean difference in daily percentage of total energy intake: –2.1 [95% CI –1.9 to –2.3]) and increased intake of polyunsaturated fat (0.6 [0.5-0.7]). The dietary counseling intervention led to greater serum proportions of polyunsaturated fatty acids ($P < .001$), with greater proportions of both circulating omega-3 ($P = .02$) and omega-6 ($P < .001$) fatty acids. The proportion of saturated fatty acids in serum was lower for both boys and girls in the intervention group ($P < .001$), whereas the serum proportion of monounsaturated fat was lower for boys in the intervention group only ($P < .001$). The intervention also reduced circulating intermediate-density lipoprotein and low-density lipoprotein lipid concentrations ($P < .01$). Dietary intervention effects on nonlipid biomarkers were minor except from greater concentrations of glutamine in the intervention group.

Conclusions Repeated dietary counseling from infancy to early adulthood yielded favorable effects on multiple circulating fatty acids and lipoprotein subclass lipids, particularly in boys. These molecular effects substantiate the beneficial role of saturated fat replacement on the metabolic risk profile.

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Trial registration ClinicalTrials.gov: NCT00223600.

The development of atherosclerosis is a lifelong process that starts in childhood and leads to cardiovascular complications in later life.[1-3] Efforts to prevent atherosclerosis at an early age are therefore justified to inhibit the establishment of cardiovascular risk factors. Central to this primordial prevention is a prudent diet aimed to prevent the development of adverse lipid levels, excess adiposity, and elevated blood pressure.[4,5]

The Special Turku Coronary Risk Factor Intervention Project (STRIP, ClinicalTrials.gov: NCT00223600) was conducted to study the effect of dietary intervention initiated in infancy and maintained until the age of 20 years on cardiometabolic risk factors.[6] It is the only randomized trial examining the health effects of reduced saturated fat diet in healthy individuals from infancy to young adulthood.[1,6] The intervention comprised repeated, individualized dietary counseling with a main focus on replacing intake of saturated fat with unsaturated fat.

BMI	Body mass index
E%	Percentage of total energy intake
HDL	High-density lipoprotein
HDL-C	High-density lipoprotein cholesterol
IDL	Intermediate-density lipoprotein
LDL	Low-density lipoprotein
LDL-C	Low-density lipoprotein cholesterol
MUFA	Monounsaturated fatty acids
NMR	Nuclear magnetic resonance
PUFA	Polyunsaturated fatty acids
SAFA	Saturated fatty acids
STRIP	The Special Turku Coronary Risk Factor Intervention Project
VLDL	Very low-density lipoprotein

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We have shown previously that the intervention is effective in decreasing saturated fat intake and leads to lower serum low-density lipoprotein cholesterol (LDL-C) concentration from infancy until 19 years of age.[7] In addition, the intervention has been associated with improved insulin sensitivity,[8] lower blood pressure,[9] enhanced brachial artery endothelial function,[2] increased ideal cardiovascular health score,[10] and reduced risk for the metabolic syndrome.[11] What is currently not well understood is the influence of reduced saturated fat intake on circulating levels of fatty acids and lipoprotein subclass measures. The dietary counseling also potentially could affect even nonlipid metabolites, such as amino acid levels and other emerging metabolic biomarkers for the risk of cardiometabolic diseases.[12]

The present study was undertaken to assess the effects of the dietary-counseling intervention on a detailed serum metabolic profile. High-throughput nuclear magnetic resonance (NMR) metabolomics provides simultaneous quantification of circulating metabolites, including fatty acids, amino acids, and detailed lipoprotein subclass profiling. This methodology has uncovered and validated novel fatty acid and nonlipid biomarkers for the risk of cardiovascular disease and type 2 diabetes.[12-16] The detailed metabolic profiling can further provide increased molecular understanding of the pathophysiology of atherosclerosis and underlying risk factors.[17-20] Here, we investigated the effects of the randomized STRIP dietary intervention trial on a comprehensive serum metabolic profile measured at 6 time points at ages 9, 11, 13, 15, 17, and 19 years in 554 participants.

Methods

The STRIP study is a prospective, randomized, infancy-onset intervention trial aiming to reduce the risk of atherosclerosis.[6,7,11] The families of 5-month-old infants were recruited to the study from well-baby clinics in Turku, Finland, between February 1990 and June 1992. When the infants were 6 months old, their families received detailed information about STRIP, and a total of 1062 infants (56.5% of the eligible age cohort) then embarked on the study (**Figure 1**; available at www.jpeds.com). At the age of 7 months, they were allocated randomly to a dietary intervention group (N = 540; 256 girls) or a control group (N = 522; 256 girls). Both groups met with a nutritionist and a pediatrician or a nurse during their study visits.

The intervention group received individualized dietary counseling at 1- to 3-month intervals until the child was 2 years of age and biannually thereafter until 20 years of age.[6,11,21] The children in the control group received only basic health education routinely given at Finnish well-baby clinics and by school health care. The control group was met biannually until 7 years of age and annually thereafter until 20 years of age.

For the present analysis, data were available from 6 time points with metabolic biomarkers quantified by high-throughput NMR metabolomics from serum samples drawn at age 9 (n = 554), 11 (n = 553), 13 (n = 508), 15 (n = 517), 17 (n = 457), and 19 (n = 417) years. This represents 92%-99% of total number of study participants. This kind of an intense intervention trial spanning over 2 decades inevitably has a substantial loss to follow-up. No systematic differences have been found between the study participants and those lost to follow-up in key characteristics, such as weight, total cholesterol, blood pressure, or saturated fat intake.[2,6,11] The study was approved by the Joint Commission on Ethics of the Turku University and the Turku University Central Hospital. Written informed consent was obtained from the parents in the beginning of the study and from the adolescents at 15 and 18 years of age.

Dietary Counseling and Food Records

The individualized dietary counseling was designed to meet the Nordic Dietary Recommendations.[22,23] The main aim was to replace saturated fat with unsaturated fat in the diet without reducing the total fat intake. The intervention aimed at fat intake of 30%-35% of daily energy (E%, or percentage of total energy intake), unsaturated to saturated fatty acid (SAFA) ratio of 2:1, and cholesterol intake of <200 mg/d. A fixed diet was never ordered but instead changes in the diet were suggested based on the child's food records (eg, replacement of dairy fat–blend spreads with vegetable oil–based spreads).

In the beginning of the intervention trial, breast feeding or formula was advised until 1 year of age, and after that, 0.5-0.6 L of skimmed milk daily was recommended for the intervention children. The intervention families were advised to add 2-3 teaspoonfuls of soft margarine or vegetable oil to the child's diet daily from 12 to 24 months of age. Quality of dietary fat was a major topic of the counseling throughout childhood and adolescence but the use of vegetables, fruits, and low-salt and whole-grain products also was recommended.[11,24] In terms of protein, specific counseling related to plant- or animal-based sources was not given. The counseling was given to the parents until the child was 7 years of age, and from then onward, gradually more information was given directly to the child. Most of the counseling material used, eg, brochures and paper-pencil tasks, was especially developed for the project due to the lack of ready-made materials for children. The parents were informed about the contents of the child's counseling sessions and encouraged to discuss the topics with the child at home.

All families (parents, caregivers) and school staff kept food records of the child's food intake. A 3-day food record was obtained every 6 months until the age of 2 years and after that, a 4-day food record was used to account for greater variation in the diet. After 7 years, the intervention children continued to keep food records biannually, and the control children kept them annually. Food records were kept for consecutive days, and they included at least 1 weekend day. During follow-up visits, the nutritionist reviewed the food records for completeness and accuracy. Nutrient intakes were analyzed with a Micro Nutrica program, developed by the Research and Development Centre of the Social Insurance Institution, Turku, Finland.[25] The data bank of the program is flexible, permitting continuous updating and additions of new single or composite foods.

Lipid and Metabolite Quantification

A high-throughput NMR metabolomics platform was used for quantification of 60 serum lipid and metabolite measures

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