

Cross-sectional associations of plasma fatty acid composition and estimated desaturase and elongase activities with cardiometabolic risk in Finnish children—The PANIC study



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KEYWORDS:

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BACKGROUND: Knowledge on the association of plasma fatty acid (FA) composition in triacylglycerol (TG) and phospholipid (PL) fractions with cardiometabolic risk in population-based samples of children is lacking.

OBJECTIVE: We investigated the associations of proportions of FA in plasma TG and PL fractions as well as estimated desaturase and elongase activities with cardiometabolic risk in a population sample of 384 children aged 6–8 years.

METHODS: Plasma FA composition was analyzed by gas chromatography. Desaturase and elongase activities were estimated as product-to-precursor FA ratios. Cardiometabolic risk was assessed using a continuous cardiometabolic risk score (CRS) variable.

RESULTS: Higher proportions of myristic and palmitoleic acids in plasma TG and PL were associated with a higher CRS. A lower proportion of linoleic acid in plasma TG was related to a higher CRS. Estimated stearoyl-CoA-desaturase and $\Delta 6$ -desaturase activities in plasma TG and PL were directly associated with CRS, whereas estimated elongase activity in plasma TG and PL was inversely related to CRS.

CONCLUSIONS: Greater proportions of myristic and palmitoleic acids and a smaller proportion of linoleic acid in plasma, as well as higher estimated stearoyl-CoA-desaturase and $\Delta 6$ -desaturase activities and a lower estimated elongase activity, are associated with cardiometabolic risk factors among children. These findings reinforce the evidence that FA metabolism is closely associated with cardiometabolic risk, starting already from childhood.

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None of the authors had a conflict of interest.

Trial registration: Clinical trial number of the PANIC Study is NCT01803776.

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Introduction

Metabolic syndrome is a cluster of cardiometabolic risk factors, such as increased waist circumference, insulin resistance, dyslipidemia, and elevated blood pressure, and it already exists among children.^{1–3} Furthermore, cardiometabolic risk factors in childhood have been associated with an increased risk of type 2 diabetes, cardiovascular diseases, and premature mortality in adulthood.^{4–6} Because the definition of metabolic syndrome in children is under wide debate,⁷ studies have commonly used continuous cardiometabolic risk scores (CRSs) to assess the accumulation of cardiometabolic risk factors in children.^{8,9}

In adults, plasma fatty acid (FA) composition has been related to the metabolic syndrome and its features, such as insulin resistance, dyslipidemia, and elevated blood pressure.^{10–14} For example, a plasma FA pattern that includes higher proportions of palmitic, palmitoleic, and dihomo- γ -linolenic acids and a lower proportion of linoleic acid has been associated with metabolic syndrome, and the mechanism behind these associations is suggested to be lower insulin sensitivity.^{15–17} In children, these types of studies have mainly been conducted in obese subjects^{18–20} and data from population-based samples are lacking. Moreover, further studies are needed to establish whether the risk in developing metabolic syndrome or diabetes could be predicted based on changes in plasma FA composition already in childhood.

There is a need to support the view that desaturase and elongase activities have an impact on cardiometabolic risk via glucose metabolism, starting in childhood. Desaturase and elongase enzymes mediate the desaturation and elongation of FA in the *de novo* lipogenesis.²¹ This *de novo* hepatic lipogenesis is a mechanism by which humans convert extra dietary carbohydrates to triacylglycerols (TG). Stearoyl-CoA-desaturase (SCD) is the key enzyme in the conversion of saturated FA to monounsaturated FA, and the ratio of palmitoleic acid to palmitic acid has been used as the estimate of its activity in earlier studies among adults, adolescents, and children.^{22–26} Two desaturation steps needed in the conversion of linoleic acid to arachidonic acid are accomplished by $\Delta 6$ -desaturase (D6D) and $\Delta 5$ -desaturase (D5D), and the ratios of γ -linolenic acid to linoleic acid and arachidonic acid to dihomo- γ -linolenic acid are used as surrogate measures of their activities, respectively. Using the calculation of these indices in studies may help understand FA metabolism in children with the accumulation of cardiometabolic risk factors.

Increased SCD and D6D activities and decreased D5D activity in plasma and erythrocyte membrane have been found to be associated with a worsened insulin sensitivity and an increased risk of type 2 diabetes in adults.^{17,26–28} However, there is no knowledge if these changes in enzyme activities occur already in childhood. Therefore, studies on the associations of estimated desaturase activities with CRS, measuring the cardiometabolic risk, in children are

needed. The results of two earlier studies among children and adolescents suggested that increased estimated D6D and decreased estimated D5D activity are associated with individual cardiometabolic risk factors such as increased plasma levels of TG and insulin and a decreased plasma level of high-density lipoprotein (HDL) cholesterol.^{23,25} To our knowledge, this study is the first one to investigate the relation of estimated elongase activity to cardiometabolic risk factors in children.

We investigated the associations of plasma FA composition, as well as estimated desaturase and elongase activities, in TG and phospholipids (PL) with CRS and single cardiometabolic risk factors in a population sample of 6–8-year old children. We hypothesized that plasma FA composition and, more specifically, higher proportions of SFA and lower proportions of polyunsaturated fatty acids (PUFA) in TG and PL are associated with higher CRS in children.

Materials and methods

Study design and study population

The present analyses are based on the baseline data of the Physical Activity and Nutrition in Children (PANIC) study, which is an ongoing physical activity and diet intervention study in a population sample of primary school children from the city of Kuopio, Finland. Altogether, 736 children aged 6–8 years of public schools of the city of Kuopio were invited to participate in the study by letters sent to the parents. Of 736 invited children, 512 (70%) participated in the baseline examinations that were conducted in 2007–2009. Based on data from the school health examination of children living in the city of Kuopio, the participants did not differ in sex distribution, age, or body mass index standard deviation score from other children who started the first grade during years 2007–2009 (data not shown). Data on plasma FA composition and cardiometabolic risk factors at baseline were available for 384 children (188 girls and 196 boys). The children and their parents gave their written informed consent. The PANIC study protocol was approved by the Research Ethics Committee of the Hospital District of Northern Savo.

Assessment of plasma FA composition

Blood sampling was conducted after a 12-hour overnight fast. Plasma FA was analyzed as described previously.^{29,30} In short, the plasma samples were extracted with chloroform-methanol (2:1), and the lipid fractions were separated by solid phase extraction with an aminopropyl column. FA in plasma TG and PL were transmethylated with 14% boron trifluoride in methanol and were analyzed by 7890A gas chromatography (Agilent Technologies, Inc., Wilmington, DE) equipped with a 25-m FFAP column. Cholesteryl nonadecanoate (Nu Chek Prep, Inc., Elysian, MA), trionadecanoin,

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