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East–west differences and migration in Finland: Association with cardiometabolic risk markers and IMT. The Cardiovascular Risk in Young Finns Study

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Abstract
Background: Coronary heart disease mortality has been internationally high in eastern Finland. The excessive mortality risk in Eastern compared with western Finns is explained by differences in cardiometabolic risk profile. Current risk profile differences and association with migration have not been reported. We examined the association of place of residence (east–west) and specifically migration with cardiometabolic risk markers and carotid intima–media thickness (IMT). Methods: The study population included 2204 participants with data available from childhood/youth in 1980 and follow-up examination in 2007. Results: Participants residing in eastern Finland in adulthood had 0.022±0.004mm higher IMT than those staying in the east (0.027±0.006mm, p<0.0001) while no difference to those continuously living in the west was found. Those who moved east-to-west had lower IMT than those staying in the east (0.027±0.006mm, p<0.0001) while no difference to those continuously living in the west was found. Those who moved east-to-west had a lower body mass index (25.3±4.3 kg/m² vs. 26.2±4.5 kg/m², p=0.01), waist circumference (85.7±12.8 cm vs. 88.6±12.8 cm, p=0.001), prevalence of metabolic syndrome (13% vs. 21%, p=0.01), and higher socioeconomic status (16.6±3.3 vs. 15.0±3.3 school years, p=0.0001) than those who stayed in the east. Conclusions: Higher IMT was found in eastern Finns than in western Finns. Participants who migrated east-to-west had a lower IMT and a better cardiometabolic risk profile than those who stayed in the east.

Key Words: Atherosclerosis, risk factors, endothelium, vascular, human migration
Introduction

Coronary heart disease (CHD) remains one of the leading causes of death globally. CHD mortality is internationally high in Finland, and men born in eastern Finland have led the world statistics of CHD mortality [1]. Eastern Finns have had higher CHD mortality than western Finns and in the Seven Countries study [2], middle-aged men in eastern Finland had the highest rate of CHD deaths related to all deaths (48%). Consequently, a national program (the North Karelia Project) was launched in order to lower CHD risk [3]. Despite advances in lifestyle and improved treatment, eastern Finns still today have approximately 20% higher CHD mortality than western Finns (National Institute for Health and Welfare; data accessed May 2013), but reasons for this difference remain obscure. The excess CHD risk in the east had earlier been explained by a higher prevalence of hypertension, smoking, and hypercholesterolemia [4]. To diminish the gap in mortality, it is important to know and repeatedly assess cardiovascular disease (CVD) risk characteristics in these groups.

The Cardiovascular Risk in Young Finns Study is an ongoing multicenter study that has followed atherosclerosis precursors in Finnish children and adolescents since 1980 (n=3596) [5]. One of the main objectives has been to study differences in cardiometabolic risk markers between eastern and western Finns. In the previous 2001 follow-up study, eastern participants had higher intima-media thickness (IMT) [6], systolic and diastolic blood pressure (SBP, DBP), and total cholesterol [7] than their western counterparts. The association of migration on these outcomes is, however, mostly unexplored. Therefore, we tested the hypotheses that participants who moved east-to-west had lower IMT and cardiometabolic risk marker levels in 2007 than those who continuously lived in the east.

Methods

Subjects

The first cross-sectional survey in the Cardiovascular Risk in Young Finns Study was conducted in 1980, when 3596 participants aged 3–18 years were randomly chosen from the national population register. The participants were examined at five study centers in Finland (university hospital cities Turku, Helsinki, Tampere, Kuopio, and Oulu, and their rural vicinities). We used data from the 27-year follow-up survey that was performed in 2007, when 2204 of the original participants attended at age 30–45 years. Participants with data on childhood and current place of residence, and total cholesterol (2007) were included in the study. In addition to risk marker and IMT data obtained in 2007, prior data since the baseline (1980) were used (Supplementary Data, eFigure1). Details of the study protocol and population have been published [5].

The study has been approved by the ethics committees of each study center, and all participants/their parents have given their written informed consents.

Place of residence

The place of residence was determined according to the subject’s study center as either eastern (Oulu and Kuopio) or western (Turku, Helsinki and Tampere) [6] (Supplementary Data, eFigure2). Geographically more accurate terms would be north-eastern and south-western, but due to historical and simplicity causes we have used the terms eastern and western. To assess if place of residence and migration are associated with cardiometabolic risk markers and IMT, the subjects were divided into four groups according to childhood (baseline) and current place of residence: those who continuously lived in the east (n=771), those who continuously lived in the west (n=1106), those who between 1980 and 2007 moved east-to-west (n=291), and those who moved west-to-east (n=25). Because of the low number of participants, those who moved west-to-east were excluded from the analyses. Most of those who moved east-to-west lived in the Helsinki area in 2007 (n=231, 79%) (Table I). The majority (n=223, 77%) of those that moved east-to-west had done so by 2001, while 23 (8%) migrated later and 45, (15%) lacked data of place of residence in 2001.
Clinical characteristics and laboratory examinations

Details of examinations have been previously described [5]. Briefly, blood pressure was measured with a random zero sphygmomanometer except at baseline examinations for 3-year-old participants for whom only SBP was recorded with an ultrasound device (Arteriosonde, Roche). Hypertension was determined as SBP $\geq$ 130 mmHg, DBP $\geq$ 85 mmHg (assessed with random zero), or the use of antihypertensive medication. Venous blood samples were drawn after an overnight fast and analyzed as described [5]. The diagnosis of type 2 diabetes included participants with fasting glucose $\geq$ 7 mmol/L or self-reported type 2 diabetes or use of medication, all in 2001 or 2007 [8]. Metabolic syndrome was defined as participant having at least three of the following risk markers: waist $\geq$ 102 cm (men)/$\geq$ 88 cm (women), fasting plasma glucose $\geq$ 5.6 mmol/L or treatment, hypertriglyceridemia $\geq$ 1.7 mmol/L, and high-density lipoprotein (HDL) cholesterol levels <1.0 mmol/L (men)/<1.3 (women), and blood pressure $\geq$ 130/$\geq$ 85 mmHg or the use of antihypertensive medication.

Lifestyle variables

Data on alcohol use, smoking, diet, physical activity, and attention paid to health habits were acquired using questionnaires. Alcohol use was assessed as standard drinks per week. Smoking was defined as current daily smoking. A healthy diet score (range 0–27, higher is better) was calculated as a combination of daily consumed portions of “healthy” and “unhealthy” foods assessed from a food frequency questionnaire [9]. A physical activity index ranging from 5 to 15 was calculated, the lower score indicating a lower activity level [10]. Attention paid to health habits was assessed on a five-point scale, where 1=pays a lot of attention, 2=pays some attention, 3=difficult to say, 4=pays little attention, 5=pays hardly any attention.

Socioeconomic status

At baseline in 1980, parental education and family income were studied with questionnaires to determine childhood socioeconomic status (SES). We assigned parental education according to the number of school years: 1 point for <9 years, 2 for 9–12 years, and 3 for >12 years. Family income was divided into quartiles and coded as 1=the lowest income quartile, 2=the second and third quartiles, and 3=the highest quartile. The participants’ own SES was determined by the self-reported amount of school years.

Ultrasound imaging

Ultrasonography was performed to measure left common carotid artery IMT using Sequoia 512 ultrasound mainframes (Acuson, Mountain View, CA) with a 13.0 MHz linear array transducer. A minimum of four measurements of the common carotid far wall were taken to derive the mean carotid IMT [13].

Statistical analyses

East–west differences in cardiometabolic risk markers and IMT in males and females were analyzed with an independent samples $t$-test. Non-normally distributed risk markers were first log-transformed. Categorical risk markers were analyzed with Fisher’s exact test. In variables that showed a significant east–west difference, an analysis of covariance (ANCOVA) was performed with separate adjustment for age and SES.

We had a particular interest in participants who had moved from east-to-west; hence, their cardiometabolic risk markers in 2007 and 1980 were compared with the other groups with an age- and sex-adjusted ANCOVA using Dunnett’s multiple comparison correction. Categorical risk markers were analyzed with a Poisson regression model with a robust error variance. $p$-Values were calculated with adjustment for sex, and a further adjustment for age, sex, and SES was also made. Sex*east–west migration interactions were studied, and if significant interaction was found the analyses were done separately for men and women. Similar analyses were performed to study the association of east–west migration with IMT. In addition to adjustment for age and sex, the analyses were further adjusted for risk factors that showed difference between the groups in 1980 or 2007.

Repeated measures linear regression analyses were used to study longitudinal trends from 1980 through 2007 between those who moved east-to-west and those who had continuously lived in the east. Models were adjusted for age and sex using a compound symmetry covariance structure.

The tests were performed with SAS version 9.3 (SAS institute, Inc, Cary, NC). Values of $p<0.05$ were considered significant.

Results

Place of residence, cardiometabolic risk markers, and intima–media thickness

Eastern participants had higher SBP and DBP, and were more often hypertensive than Western participants (Table II). Women living in the east had
higher serum total and LDL cholesterol, apoB, triglycerides, insulin, and prevalence of metabolic syndrome than western women. Western women had a higher diet score, indicative of a healthier diet, than eastern women. There were more smokers among eastern men than western men but their consumption of alcohol was lower. SES was higher in the west in both men and women. All differences were independent of age. Because of the significant east–west difference in SES the prior analyses were also adjusted for adulthood SES. With this adjustment, the difference in smoking disappeared (data not shown).

IMT was higher in the east than in the west (0.642±0.003 vs. 0.620±0.002 mm, p<0.0001, adjusted for age and sex). There was no sex*place-of-residence interaction, indicating that place of residence had a similar association with IMT in both sexes. The difference between eastern and western participants remained significant after adjustment for SES. IMT had also increased more between 2001 and 2007 in eastern than in western participants (0.058±0.003 vs 0.041±0.002 mm, p<0.0001; IMT in 2001 included in the analysis).

The effect of east–west migration

Cardiometabolic risk markers in 2007. Compared with participants who continuously lived in the east, those who moved east-to-west between 1980 and 2007 had lower BMI, waist circumference, insulin concentration, SBP, DBP, prevalence of hypertension, and metabolic syndrome in 2007 (Table III). Those who moved east-to-west also had a higher diet score and SES, were less often smokers, and paid more attention to health habits than participants who stayed in the east.

Compared with participants who continuously lived in the west, those who moved east-to-west had lower BMI and waist circumference and higher SBP and DBP than participants who continuously lived in the west. The participants who moved east-to-west also had a higher diet score and SES, and physical activity index and they paid more attention to health habits than those who continuously lived in the west.

Age and sex were included in all previous analyses. Because of the significant difference in SES between participants who migrated east-to-west and those who continuously lived in the east or in the west, the prior analyses were also adjusted for adulthood SES. With this adjustment, the differences between the
groups in smoking and physical activity were no longer significant. Regarding diet score, the difference between those who moved east-to-west and those who continuously lived in west disappeared (data not shown for the analyses adjusted with SES).

There was a significant sex*east–west migration interaction in total, HDL and LDL cholesterol, apoB, triglycerides, and insulin, suggesting that the associations between the migration groups and these outcomes were different in males and females. Therefore, these variables were analyzed separately for the sexes. In men, no differences between the groups were detected (Supplementary Data, etable I). In women, those who moved east-to-west had lower total and LDL cholesterol, apoB, triglycerides, and insulin, and higher HDL cholesterol than those who stayed in the east. Compared with women who continuously lived in the west, those who moved east-to-west had lower insulin and apoB, and higher HDL cholesterol.

**Intima-media thickness in 2007.** The participants who moved east-to-west had lower IMT than those who continuously lived in east (Figure 1a). This difference remained when the risk markers that were different between the groups in 2007 (Figure 1b), and also in 1980 (Figure 1c) were included in the analyses. The IMT of those who moved east-to-west was similar to those who continuously lived in the west. The IMT progressed less between 2001 and 2007 in those who moved east-to-west than in those who continuously lived in the east (0.027±0.005 vs. 0.058±0.003 mm, \( p < 0.0001 \)) (adjusted for age, sex, and IMT in 2001).

### Baseline (1980) cardiometabolic risk markers

Among participants who lived in eastern Finland at baseline but had moved east-to-west by 2007, SBP was lower and their parents’ education and family income were higher at baseline than among subjects who stayed in the east (Table IV). Participants who moved east-to-west also had lower BMI at baseline than participants who lived in the west, both 1980 and 2007. Instead, their DBP and apoB were higher, and apoA concentrations were lower than among those who continuously lived in the west. Interaction between sex and

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<table>
<thead>
<tr>
<th>Table III. Effect of east–west migration: Cardiometabolic risk markers in 2007. The probability values show significance compared with the east 1980 west 2007 group, adjusted for sex and age.</th>
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<td>Alcohol consumption (drinks per week)a</td>
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<td>Physical activity index (range 5–15)</td>
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<td>Attention paid to health habitsc</td>
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<td>SES (school years)</td>
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*aMean±SD or median (interquartile range).  
*cLower is better.
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East-to-west migration was significant at baseline in total and LDL cholesterol; women who had moved east-to-west had lower LDL cholesterol (3.45 vs. 3.61 mmol/L, \( p = 0.03 \)) and tendency for lower total cholesterol (5.33 vs. 5.49 mmol/L, \( p = 0.07 \)) in 1980 than women who continuously lived in the east while no associations were found in men.

Because there were differences at baseline between those who moved east-to-west and those who stayed in the east, we also reanalyzed the risk markers in 2007 (Table III) between these two groups with adjustment for risk factors that differed between the groups at baseline (SBP, parental income, and parental education). The results were essentially similar; only BMI lost its statistical significance.

Cardiometabolic risk markers from 1980 to 2007. Because of special interest in those of eastern origin, longitudinal differences from 1980 to 2007 in the cardiometabolic risk markers shown in Table III were studied between participants who moved east-to-west and those who continuously lived in the east. Participants who moved east-to-west had lower BMI, SBP and DBP, and insulin concentration during the follow-up (Supplementary data, eFigure 3a–d). These associations were similar in both sexes (sex*group interactions).
non-significant). There was a significant sex*group interaction in apoB, total cholesterol and LDL cholesterol; higher levels in participants who continuously lived in east were found in women (Supplementary data, eFigure 3e–g) but not in men (data not shown).

Discussion

We found that participants who had migrated from east-to-west between 1980 and 2007 had lower IMT in 2007 than participants who stayed in the east, but no difference to those who continuously lived in the west was found. Those who moved east-to-west had lower BMI and waist circumference than those who continuously lived either in the east or in west. In all, differences in the cardiometabolic risk markers were more pronounced in women than men.

Twenty-seven percent of those who lived in the east in 1980 had moved to the west by 2007, indicating that migration in our study population has been substantial. In addition to differences in IMT and cardiometabolic risk markers, participants who moved east-to-west had higher adulthood SES and a healthier lifestyle (e.g., smoking and diet) than participants continuously living in the east or the west. Our research indicates that the higher SES among participants who moved east-to-west contributed to their healthier lifestyle. Previous studies have found the association of higher SES with better health awareness and cardiometabolic risk markers [14,15].

The higher SES, healthier lifestyle, and better cardiometabolic risk profile likely contributed to IMT being lower among those who moved east-to-west than among those who stayed in the east. However, the IMT difference remained after adjustment for these factors, suggesting that other mediators likely exist. We have previously observed in the same cohort that carotid IMT increases 0.0057±0.0004 mm/year [13]. Applying the vascular age concept [16], the IMT difference between participants who moved east-to-west and those who stayed in the east (0.0265 mm) corresponds to a difference of 4.7 years in vascular age.

At baseline (1980) when still living in the east, SBP was lower and parental SES was higher among the participants who later migrated east-to-west than in those who stayed in the east. In longitudinal analyses from 1980 to 2007, those who moved east-to-west had lower SBP, DBP, BMI, and insulin than participants who stayed in the east. It thus seems that the migrating individuals and families were already healthier at baseline. This observational study cannot establish whether the east-to-west migration has beneficially influenced the cardiometabolic risk profile or whether those with lower risk profile have been more prone to migrate. The data mainly support the latter explanation.

Regarding differences between eastern and western Finns, our study gives further support to earlier studies which have found that the differences in cardiometabolic risk markers have narrowed, especially in serum lipids [17]. DBP had earlier been found to decrease steeper in eastern Finland than in western Finland [18]. Lower SBP and DBP in the west than in the east was found in this study, as reported earlier from the Young Finns cohort [6]. Accurate assessment of blood pressure is prone to many factors potentially causing bias, e.g., the random-zero sphygmomanometer used here is suggested to be sensitive to methodological challenges [19]. Thus, the east–west differences in blood pressure should be interpreted with caution. Previously, we have shown higher IMT in men living in Sweden who originated from eastern Finland than those originating from western Finland [20]. We observed higher IMT among participants living in the east compared than those in the west.

Men who had moved from eastern to western Finland were found to have higher risk of atherosclerosis in the left coronary artery [21] and sudden cardiac death than men born in the west [22]. We could not study the effect of east-to-west migration on CVD risk because of our young study population but those who moved east-to-west had no difference in IMT to those who continuously lived in the west. Moreover, those who moved east-to-west had lower IMT than those who continuously lived in the east. Migration having a positive association with cardiometabolic health has been found previously. In Great Britain, men who had moved from other parts of the country to the south, which is the area of lowest CVD mortality rate, have been shown to have similar risk of CVD mortality to men born in the south [23]. Examples of adverse effects of migration are more common. Urban Chinese living in Hong Kong or Australia have been found to have higher IMT than people living in rural China [24]. Hawaii men with Japanese ancestry have been found to have an excessive CHD risk compared with men living in Japan [25].

Limitations of this study include loss of follow-up, inevitable in all long-term studies. Because of the wide age range at original enrolment of the subjects (3–18 years), a large proportion of subjects lacked data on early childhood [5]. Moreover, our classification of participants as those who migrated or not is based on information of their place of residence from two time-points (1980 and 2007) and does not consider the possibility that some participants may have moved several times between these time-points, nor does it consider at which time the migration occurred.
Because our main analyses were adjusted with age, the findings are not due to age distribution differences. Future studies should investigate whether the cardiometabolic risk profile and IMT differences between eastern and western Finns persist and whether the present differences are associated with future clinical end-points. Further, examination of long-term consequences of migration and consideration of genetic east–west differences influencing cardiometabolic risk profile differences are also needed. This study suggests that the geographic difference in CHD mortality in Finland and presumably globally can be targeted by focusing on CHD risk marker levels and lifestyle intervention.

In summary, our study shows that Finns who migrated east-to-west had lower IMT than those who continuously lived in the east while no difference to those who continuously lived in the west was detected. We conclude that the cardiometabolic risk profile in 2007, at baseline (1980) and in longitudinal analyses from 1980 to 2007 was better in those who moved east-to-west than in those who stayed in the east.

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Conflict of interest
None declared.

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Supplemental material
Online supplementary data is available at http://sип. sagepub.com/supplemental

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