Association of Cardiorespiratory Fitness with Vascular Intima-Media Thickness, Elasticity and Fatty Liver in Young Adults

Prospective Special Turku Coronary Risk Factor Intervention Project (STRIP)

Roope Raekumpu

Syventävien opintojen kirjallinen työ

Kevätlukukausi 2026

Association of Cardiorespiratory Fitness with Vascular Intima-Media Thickness, Elasticity and Fatty Liver in Young Adults

Prospective Special Turku Coronary Risk Factor Intervention Project (STRIP)

Roope Raekumpu

Kevätlukukausi 2026

Sydäntutkimuskeskus ja Väestötutkimuskeskus

Vastuuhenkilöt: prof. Katja Pahkala, prof. Markus Juonala ja dos. Tomi Laitinen

UNIVERSITY OF TURKU Faculty of Medicine

Research Centre of Applied and Preventive Cardiovascular Medicine and
Centre for Population Health Research

Association of Cardiorespiratory Fitness with Vascular Intima-Media Thickness,
Elasticity and Fatty Liver in Young Adults

Roope Raekumpu
Advanced Studies Thesis, Spring Semester 2026

Abstract

The development of cardiovascular diseases and metabolic-associated fatty liver disease (MASLD) originates in youth. This study aimed to investigate the cross-sectional and longitudinal associations of cardiorespiratory fitness with aortic and carotid intima-media thickness (IMT), arterial elasticity, and the occurrence of fatty liver in young adults at the age of 26 years. Additionally, the sustained effect of a 20-year infancy-onset lifestyle intervention (STRIP cohort) on fitness and common metabolic risk factors were evaluated.

This study is a part of the prospective STRIP cohort. Maximal oxygen uptake (VO_{2max}) was measured using a cycle ergometer at the ages of 17 and 26 years. Aortic and carotid IMT, arterial elasticity, and hepatic steatosis were assessed via ultrasonography at the ages of 17 and 26 years. Statistical models were adjusted primarily for sex. Further adjustments were made for the STRIP study group and several cardiometabolic and socioeconomic risk factors.

Belonging to the STRIP intervention group was associated with higher cardiorespiratory fitness at the age of 26 years. Fitness at the age of 26 years was directly associated with a thickening of carotid IMT during the 9-year time-period from the age of 17 to 26 years, which remained significant after full adjustments for cardiometabolic risk factors. Longitudinal change in fitness from the age of 17 to 26 years was associated with longitudinal changes in aortic IMT and elasticity, but these associations were attenuated after full adjustment for cardiometabolic risk factors. Low fitness at the ages of 17 and 26 years strongly predicted the occurrence of fatty liver at age 26, with the vast majority of cases clustering in the lowest fitness tertile. Higher fitness at the age of 17 years independently and significantly predicted a lower risk of fatty liver at the age of 26 years (OR [0.824], 95% CI [0.717] – [0.948], after adjusting for sex, STRIP intervention/control group and BMI. The cross-sectional association at the age of 26 years followed a similar trend but reached a borderline significance after full adjustment for sex, STRIP intervention/control group and BMI (OR [0.855], 95% CI [0.731] – [1.000]).

Cardiorespiratory fitness is a robust, independent protective factor against fatty liver during the transition to young adulthood. The favorable associations between fitness and vascular structure previously observed in this cohort at the age of 17 years did not persist independently into young adulthood. The observed carotid thickening in fit young adults, unaccompanied by decreased elasticity, suggests physiological vascular remodeling referred to as the 'athlete's artery', rather than pathological aging. Furthermore, long-term, early-life lifestyle counseling provides latent benefits for cardiorespiratory health in young adulthood.

Keywords: cardiorespiratory fitness, fatty liver, arterial elasticity, intima-media thickness, young adults

INTRODUCTION

Cardiovascular diseases (CVDs) remain the leading cause of morbidity and premature mortality globally.[1] Although clinical manifestations typically appear in middle age or later, the initiation and progression of the atherosclerotic process begin as early as childhood.[2,3] This lifelong developmental process is characterized by adverse structural and functional changes in the arterial wall[4], which often precede clinical symptoms by decades.[5,6] Primordial prevention, aimed at preventing the emergence of risk factors in early life, is therefore a critical strategy for reducing the lifelong burden of CVD.

High-resolution ultrasonography provides a non-invasive methodology to assess subclinical markers of atherosclerosis, such as increased arterial intima-media thickness (IMT) and decreased arterial elasticity.[7–9] Increased IMT and arterial stiffness are recognized as independent predictors of future cardiovascular events and higher cardiovascular mortality in adults.[8,10–12] While these associations are well-established in older populations,[13,14] the determinants of vascular health in children and young adults require further investigation.

Cardiorespiratory fitness (later fitness), defined as the capacity of the respiratory and circulatory systems to supply oxygen to skeletal muscles during physical activity, is a potent indicator of overall health.[15–18] Fitness is strongly interrelated with physical activity (PA), but it is important to note that they are not synonyms. However, physical activity needs to be of sufficient intensity to improve fitness levels. Furthermore, fitness is also influenced by genetics, which may explain as much as half of the interindividual variance in VO2max.[19,20] Consequently, similar physical activity levels or exercise training can yield different fitness levels individually. In children and adolescents, the association between physical activity and fitness is typically weak to moderate.[21] Despite these complexities, fitness has been shown to track significantly from adolescence to young adulthood (rank-order correlation coefficient = 0.60-0.62) suggesting that fitness levels in youth are strong predictors of health in later life.[22]

The relationship between fitness and vascular structure appears to be site-specific during early life. We previously reported that in 17-year-old adolescents, fitness was favorably associated with IMT and elasticity in the abdominal aorta, but no such association was observed in the carotid artery.[23] The abdominal aorta is one of the earliest sites for atherosclerotic lesions, making it a potentially more sensitive marker of subclinical changes in youth.[24] However, some evidence suggests that high training intensity can be associated with localized increases in carotid IMT, a physiological remodeling phenomenon often conceptualized as the "athlete's artery".[25,26] In this context, thickening occurs as a compensatory adaptation to hemodynamic loading without a concomitant loss of elasticity.

In addition to vascular health, fitness is increasingly recognized for its role in preventing metabolic dysfunction-associated steatotic liver disease (MASLD), formerly referred to as non-alcoholic fatty liver disease.[27] MASLD is a rapidly expanding global concern, closely linked to obesity and insulin resistance. Evidence suggests a robust inverse relationship between fitness and liver fat content, often independent of BMI.[28,29] Good fitness may therefore provide a "metabolic buffer" that protects against hepatic steatosis even in the presence of adiposity.

Despite the importance of these markers, longitudinal data examining the transition from adolescence into young adulthood remain scarce. The STRIP cohort, with its unique 20-year infancy-onset dietary intervention and long-term follow-up, provides an exceptional framework to address this gap.[30,31] The primary aim of this study was to investigate the cross-sectional (N = 296) and longitudinal (N = 148) associations of fitness with aortic and carotid IMT, arterial elasticity, and the occurrence of fatty liver in participants followed from the age of 17 to 26 years. Furthermore, we aimed to evaluate whether the 20-year lifestyle counseling intervention has a sustained, latent effect on fitness and cardiometabolic outcomes in young adulthood.

METHODS

Study Design and Subjects:

The present study is part of the prospective, randomized Special Turku Coronary Risk Factor Intervention Project (STRIP).[30,31] The STRIP study was designed to investigate the effects of long-term dietary and lifestyle counseling, initiated in infancy, on the development of atherosclerosis risk factors. Families of 6-month-old infants were recruited between February 1990 and June 1992 by nurses at Turku City well-baby clinics. At the age of 7 months, 1062 infants (56.5% of the eligible age-cohort) were randomly allocated to either a dietary intervention group (n = 540) or a control group (n = 522). The intervention group received individualized dietary counseling from a nutritionist at least biannually until the age of 20, focusing on reducing the intake of saturated fat and cholesterol. Additionally, child-oriented antismoking counseling was initiated at age 8. The control group received the standard health education provided at Finnish well-baby clinics and school health care. The study protocol was approved by the Joint Commission on Ethics of the University of Turku and Turku University Central Hospital. Written informed consent was obtained from the parents at the beginning of the study and from the participants at age 15.

The current study population comprises young adults for whom measures of cardiorespiratory fitness and arterial phenotypes (IMT and elasticity) were available at the age of 17 and/or 26 years. At the age of 17 years, cardiorespiratory fitness data were available for 378 participants, while aortic and carotid ultrasound measures were provided for 463 and 498 adolescents, respectively. At the 26-year follow-up, fitness was measured in 298 participants, and aortic and carotid measures were available for 521 and 526 participants, respectively. Longitudinal data for cardiorespiratory fitness at both time points were available for 156 subjects. Of these, 136 and 148 subjects had concurrent aortic and carotid measurements, respectively, at both ages to allow for the assessment of longitudinal changes. Fatty liver ultrasonographic data (measured at the age of 26 years) concurrent with fitness measures were available for 270 and 296 participants at ages of 17 and 26 years, respectively.

Vascular IMT and Elasticity

IMT and elasticity of abdominal aorta and common carotid artery were studied with ultrasonography (Acuson Sequoia 512 mainframe; Acuson, Mountain View, CA) biyearly from the age of 11, till the age of 19, and then again in the follow-up study at the age of 26, when aortic and carotid ultrasound measures were available for 521 and 526 participants, respectively.[32,33] For aortic IMT measurements, the most distal 15 mm of abdominal aorta was scanned with a ≥10 MHz linear-array transducer. The image was focused on the dorsal wall, captured, and stored for subsequent offline analysis. Four measurements of IMT covering the far wall were taken and the average was used. In our laboratory, interobserver coefficient of variation (CV) was 3.9% (n = 88) and between-visits CV was 4.9% (n = 21).[34]

To assess carotid IMT, the far wall of the distal common carotid arteries on both sides 1 to 2 cm from the bulb were scanned from anterior oblique and lateral angles using a 13-MHz linear-array transducer. Two end-diastolic frames from both interrogation angles on both sides were analyzed. Four measures were obtained in each image; the mean indicated average carotid IMT. In our laboratory, interobserver variation was 3.0% (n = 88), and between-visit CV was 3.9% (n = 21).[34]

Elasticity of aortic and carotid arteries was assessed using M-mode images and concomitant measurement of blood pressure in the brachial artery.[32] Arterial diameter was measured twice at end diastole and twice at end systole. Mean of the end-diastolic and end-systolic diameters, along with blood pressure and IMT, were used to calculate arterial elasticity indices: distensibility and Young's elastic modulus (YEM). Higher compliance and lower YEM value indicate greater arterial elasticity. Aortic and carotid elasticity indices, respectively, were closely correlated (aortic compliance and YEM: r = –0.88, P < .0001; carotid compliance and YEM: r = –0.80, P < .0001).[23]

Ultrasonography studies were performed in silence in a temperature-controlled clinical research laboratory. On measurement day, test subjects were advised to refrain from smoking, caffeinated drinks, juice, high-fat meals, and vitamin supplementation.

Fitness

Fitness (maximum oxygen uptake [VO2max], mL/kg/min) was measured with maximal cycle ergometer exercise test (Ergoselect 100 K; Ergoline, Bitz, Germany).[35] The test began at a workload of 50 W, which was increased by 30 W (boys)/25 W (girls) every 2 minutes until exhaustion. Mean workload during the last 4 minutes of work was calculated and VO2max was estimated as recommended by the American College of Sports Medicine.[36]

Sex-specific tertile cutoff points were calculated at each age point to classify participants into low, moderate, and high fitness groups. To demonstrate the longitudinal change in fitness from adolescence to young adulthood, delta-variables were created for participants with available data at both time points. These delta-variables were systematically calculated by subtracting the values measured at the age of 17 years from the values measured at the age of 26 years, such that a positive value indicates an improvement in cardiorespiratory fitness over the nine-year follow-up.

Physical Activity

Leisure-time physical activity (LTPA) was assessed with a self-administered questionnaire, and calculated by multiplying mean frequency, duration, and intensity (multiple of resting metabolic rate; metabolic equivalent [MET]) of weekly LTPA (MET h/wk).[37,38] LTPA comprised recreational and organized physical activity/sports outside work hours. The questionnaire correlates moderately well with objective physical activity measures.[39] LTPA of 30 MET h/wk corresponds to ∼1 hour of moderate-intensity physical activity daily, recommended as the minimum amount of physical activity for young adults; 10 MET h/wk corresponds to ∼2 hours of moderate intensity physical activity weekly and indicates a low LTPA level in young adults.[39]

Physical Examination and Smoking

Height and weight were measured, and BMI calculated as weight/height^2 (kg/m^2). Blood pressure was measured 3 times (mean used) from the right arm with an automated sphygmomanometer during the ultrasonography study (Omron M4; Omron Matsusaka, Matsusaka, Japan).[23] Smoking habits were assessed with a questionnaire in which the test subjects reported as either a regular smoker or not a regular smoker. Regular smoking was defined as smoking at least once per day at the time of the 26-year follow-up visit.[40] Evaluation of smoking in this matter did not separate people who had quit smoking at some point from those who had never smoked. Of those participants who also had measures from the cycle ergometer test, there were 13 regular smokers and 278 non-smokers.

Laboratory Measurements

A fasting venous blood sample was drawn, and concentrations of serum total and high-density lipoprotein (HDL) cholesterol, triglyceride, and insulin and glucose were determined.[41] Low-density lipoprotein (LDL) cholesterol concentration was calculated by using the Friedewald formula. HOMA-IR (homeostasis model assessment of insulin resistance) was calculated as fasting insulin (µU/mL) × fasting glucose (mmol/L)/22.5. High-sensitivity C-reactive protein (hs-CRP) was assayed by a turbidimetric immunoassay with sensitivity of 0.06 mg/L.[38]

Fatty Liver

Ultrasonographic imaging of the liver was performed with validated protocol[42] between 2015 and 2018 with for 26-year-old participants by using Sequoia 512 ultrasound mainframes (Acuson, Mountain View, CA) with 4.0-MHz adult abdominal transducers.[43] Evaluation of fatty liver was performed according to liver-to-kidney contrast, parenchymal brightness, deep beam attenuation and bright vessel walls.[44] The liver-to-kidney contrast was determined as a clear ultrasonographic contrast between the hepatic parenchyma and the right renal cortex. Parenchymal brightness was defined as hyperechogenic liver tissue with fine, tightly packed echoes on ultrasound examination. Deep beam attenuation was defined as an indistinguishable diaphragm line, and bright vessel walls were defined as the presence of brightly visible walls of small intrahepatic vessels. According to these criteria, the presence of fatty liver was assessed visually from nonblinded images by a trained ultrasonographer who was masked to participant's characteristics. Full details of the study design have been published. At the age of 26 years, fatty liver was present in 16 / 270 (5.9%) participants with fitness data from the age of 17 years, and 14 / 296 (4.7%) with fitness data from the age of 26 years. All 16 cases with age-17 fitness data, and 12 / 14 with age-26 fitness data, were in the lowest fitness tertile.

Socioeconomic Status (SES)

Sociodemographic characteristics in early adulthood were assessed with a questionnaire at the age of 26 years. The participants' actualized educational level was classified into three categories: low (1 = elementary school, high school, or vocational school), intermediate (2 = bachelor's degree or university courses without a final degree), and high (3 = master's degree, licentiate, or doctorate). Because a proportion of the young adults were still studying at the time of the 26-year follow-up, a projected educational level was also determined. In this projected assessment, university students currently pursuing a full degree were elevated to the high education category (group 3) under the assumption of future graduation. Participants taking university courses without the intention of completing a full degree remained in the intermediate category (group 2).

Furthermore, to form a comprehensive measure of childhood socioeconomic background, an overall SES-index was constructed based on parental education and income. The educational level of the more highly educated parent was assessed on a 10-point scale (ranging from 0 =

studying at the moment, to 9 = doctoral degree). The gross monthly income of the parent with the higher income was categorized on a 6-point scale (0 = 0–1999 €, 1 = 2000–3999 €, 2 = 4000–5999 €, 3 = 6000–7999 €, 4 = 8000–9999 €, and 5 = >10 000 €). To assign equal mathematical weight to both variables, the initial scores were proportionally scaled to share an identical maximum value of 6. The scaled scores were then summed, resulting in a continuous childhood SES-index ranging from a minimum of 0 to a maximum of 12. In the present study population, the median of this derived index was approximately 6.

Statistical Analyses

Statistical analyses were performed using SAS software version 9.4 (TS1M8, SAS Institute Inc., Cary, NC, USA). The normality of variable distributions was assessed using visual inspection of histograms and formal univariate tests. Due to skewed distributions, logarithmic transformations were applied to variables representing carotid and aortic elasticity (Young's Elastic Modulus, YEM), aortic and carotid compliance, weight, BMI, waist circumference, triglycerides, glucose, insulin, HOMA-IR, hs-CRP and alcohol consumption prior to statistical modeling to satisfy the assumption of normality.

Multivariate linear regression analysis was used to study associations of 1) fitness with vascular phenotypes as well as cardiometabolic risk factors and behaviors, 2) associations between change in fitness and change in vascular phenotypes over the 9-year follow-up, and 3) interaction between fitness and the outcome variables. Associations of fitness with categorical outcome measures were studied with logistic regression analysis with covariates.

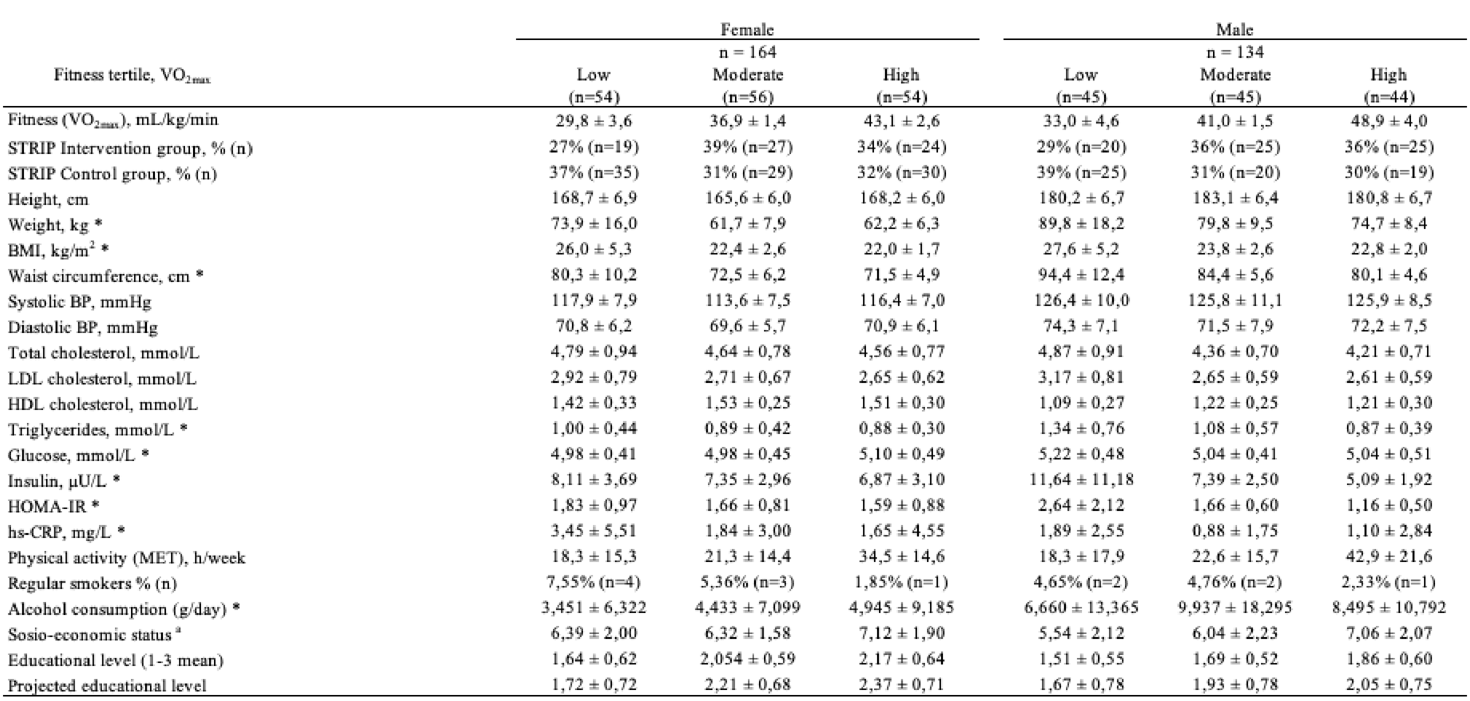
All models were primarily adjusted for sex. Further adjustments for cardiometabolic risk factors (BMI, diastolic blood pressure, total cholesterol, triglycerides, LTPA, insulin, hs-CRP), and STRIP intervention/control group, SES-index, and the projected educational level.

RESULTS

Fitness and Cardiovascular Risk Factors

Characteristics of the study population are shown in Table 1. Means of the cardiometabolic risk factors and behaviors are presented in the fitness tertiles among females and males at the age of 26 years.

TABLE 1 Characteristics of the study population at the age of 26 years, categorized by sex-specific fitness tertiles.



Fitness tertile, VO_{2max}	Female n = 164 Low (n=54)	Moderate (n=56)	High (n=54)	Male n = 134 Low (n=45)	Moderate (n=45)	High (n=44)
Fitness (VO_{2max}), mL/kg/min	29,8 ± 3,6	36,9 ± 1,4	43,1 ± 2,6	33,0 ± 4,6	41,0 ± 1,5	48,9 ± 4,0
STRIP Intervention group, % (n)	27% (n=19)	39% (n=27)	34% (n=24)	29% (n=20)	36% (n=25)	36% (n=25)
STRIP Control group, % (n)	37% (n=35)	31% (n=29)	32% (n=30)	39% (n=25)	31% (n=20)	30% (n=19)
Height, cm	168,7 ± 6,9	165,6 ± 6,0	168,2 ± 6,0	180,2 ± 6,7	183,1 ± 6,4	180,8 ± 6,7
Weight, kg *	73,9 ± 16,0	61,7 ± 7,9	62,2 ± 6,3	89,8 ± 18,2	79,8 ± 9,5	74,7 ± 8,4
BMI, kg/m^2 *	26,0 ± 5,3	22,4 ± 2,6	22,0 ± 1,7	27,6 ± 5,2	23,8 ± 2,6	22,8 ± 2,0
Waist circumference, cm *	80,3 ± 10,2	72,5 ± 6,2	71,5 ± 4,9	94,4 ± 12,4	84,4 ± 5,6	80,1 ± 4,6
Systolic BP, mmHg	117,9 ± 7,9	113,6 ± 7,5	116,4 ± 7,0	126,4 ± 10,0	125,8 ± 11,1	125,9 ± 8,5
Diastolic BP, mmHg	70,8 ± 6,2	69,6 ± 5,7	70,9 ± 6,1	74,3 ± 7,1	71,5 ± 7,9	72,2 ± 7,5
Total cholesterol, mmol/L	4,79 ± 0,94	4,64 ± 0,78	4,56 ± 0,77	4,87 ± 0,91	4,36 ± 0,70	4,21 ± 0,71
LDL cholesterol, mmol/L	2,92 ± 0,79	2,71 ± 0,67	2,65 ± 0,62	3,17 ± 0,81	2,65 ± 0,59	2,61 ± 0,59
HDL cholesterol, mmol/L	1,42 ± 0,33	1,53 ± 0,25	1,51 ± 0,30	1,09 ± 0,27	1,22 ± 0,25	1,21 ± 0,30
Triglycerides, mmol/L *	1,00 ± 0,44	0,89 ± 0,42	0,88 ± 0,30	1,34 ± 0,76	1,08 ± 0,57	0,87 ± 0,39
Glucose, mmol/L *	4,98 ± 0,41	4,98 ± 0,45	5,10 ± 0,49	5,22 ± 0,48	5,04 ± 0,41	5,04 ± 0,51
Insulin, µU/L *	8,11 ± 3,69	7,35 ± 2,96	6,87 ± 3,10	11,64 ± 11,18	7,39 ± 2,50	5,09 ± 1,92
HOMA-IR *	1,83 ± 0,97	1,66 ± 0,81	1,59 ± 0,88	2,64 ± 2,12	1,66 ± 0,60	1,16 ± 0,50
hs-CRP, mg/L *	3,45 ± 5,51	1,84 ± 3,00	1,65 ± 4,55	1,89 ± 2,55	0,88 ± 1,75	1,10 ± 2,84
Physical activity (MET), h/week	18,3 ± 15,3	21,3 ± 14,4	34,5 ± 14,6	18,3 ± 17,9	22,6 ± 15,7	42,9 ± 21,6
Regular smokers % (n)	7,55% (n=4)	5,36% (n=3)	1,85% (n=1)	4,65% (n=2)	4,76% (n=2)	2,33% (n=1)
Alcohol consumption (g/day) *	3,451 ± 6,322	4,433 ± 7,099	4,945 ± 9,185	6,660 ± 13,365	9,937 ± 18,295	8,495 ± 10,792
Sosio-economic status [a]	6,39 ± 2,00	6,32 ± 1,58	7,12 ± 1,90	5,54 ± 2,12	6,04 ± 2,23	7,06 ± 2,07
Educational level (1-3 mean)	1,64 ± 0,62	2,054 ± 0,59	2,17 ± 0,64	1,51 ± 0,55	1,69 ± 0,52	1,86 ± 0,60
Projected educational level	1,72 ± 0,72	2,21 ± 0,68	2,37 ± 0,71	1,67 ± 0,78	1,93 ± 0,78	2,05 ± 0,75

Descriptive data: means ± SD, % (n). BP, blood pressure; LDL, Low Density Lipoprotein; HDL, High Density Lipoprotein; hs-CRP, high-sensitivity C-reactive protein; MET, Metabolic equivalent of task; na, not applicable.

[a] *Family income and parent level of education in equally weighted index.*

Table 2 describes the associations of fitness, treated as a continuous variable, with STRIP study group (intervention/control) as well as with cardiometabolic risk factors and behaviors, adjusted for sex, at the age of 26 years. Participants who belonged to the STRIP intervention group had a higher fitness level compared with those in the control group. Fitness was inversely associated with weight, waist circumference, BMI, systolic and diastolic blood pressure, and concentrations of total cholesterol, LDL-cholesterol, triglycerides and hs-CRP. In line, fitness was inversely associated with levels of insulin and HOMA-IR. Fitness was directly associated with HDL-cholesterol, LTPA, socioeconomic status, as well as current and projected educational levels at the age of 26 years. There were no associations between fitness and smoking or alcohol usage.

Significant sex interaction was found for insulin, HOMA-IR and hs-CRP. The associations observed between fitness and the above factors remained after the analyses were conducted separately for females and males (Table 2).

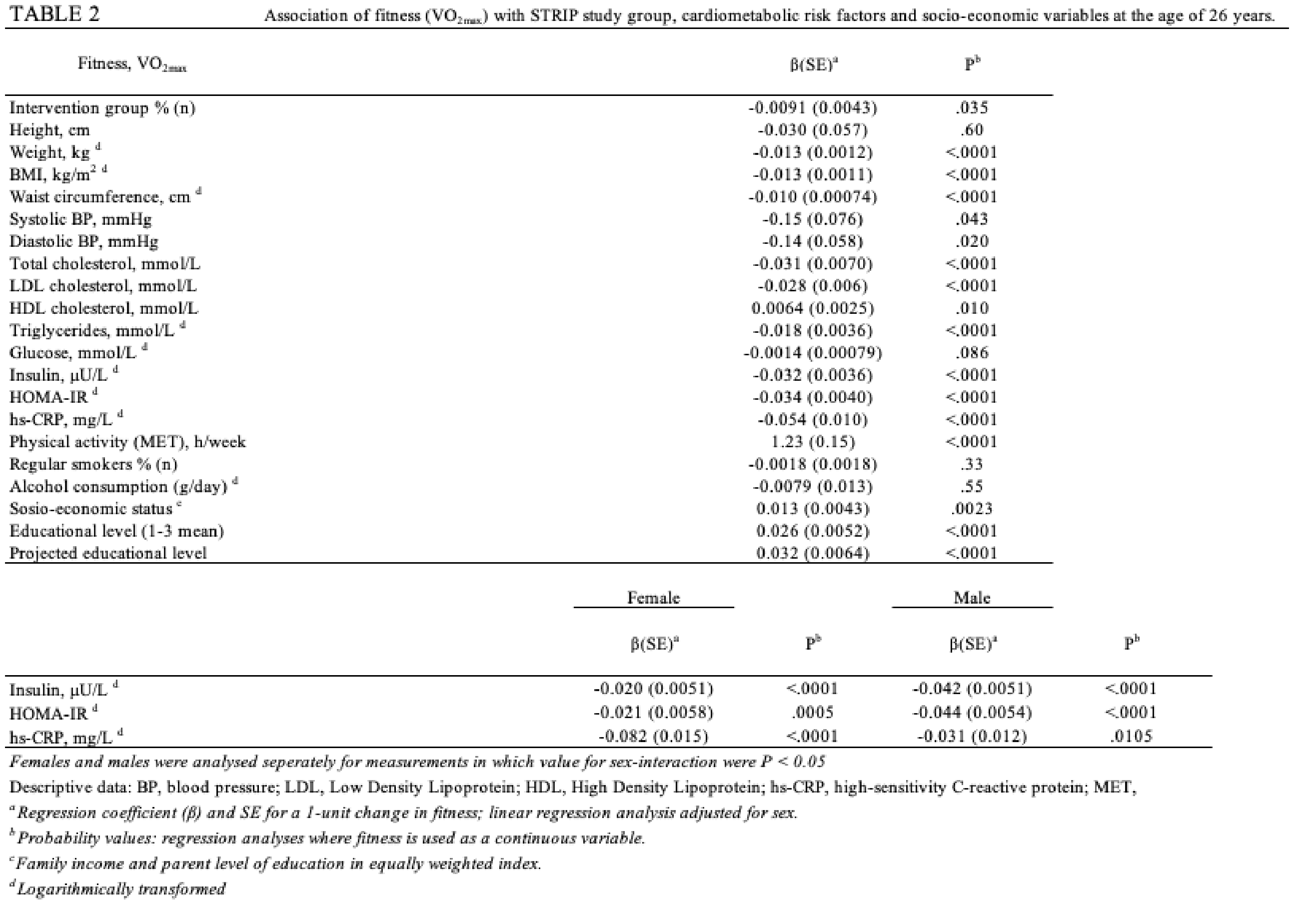


TABLE 2 Association of fitness (VO_{2max}) with STRIP study group, cardiometabolic risk factors and socio-economic variables at the age of 26 years.

Fitness, VO_{2max}	β(SE)[a]	P[b]
Intervention group % (n)	-0.0091 (0.0043)	.035
Height, cm	-0.030 (0.057)	.60
Weight, kg [d]	-0.013 (0.0012)	<.0001
BMI, kg/m^2 [d]	-0.013 (0.0011)	<.0001
Waist circumference, cm [d]	-0.010 (0.00074)	<.0001
Systolic BP, mmHg	-0.15 (0.076)	.043
Diastolic BP, mmHg	-0.14 (0.058)	.020
Total cholesterol, mmol/L	-0.031 (0.0070)	<.0001
LDL cholesterol, mmol/L	-0.028 (0.006)	<.0001
HDL cholesterol, mmol/L	0.0064 (0.0025)	.010
Triglycerides, mmol/L [d]	-0.018 (0.0036)	<.0001
Glucose, mmol/L [d]	-0.0014 (0.00079)	.086
Insulin, μU/L [d]	-0.032 (0.0036)	<.0001
HOMA-IR [d]	-0.034 (0.0040)	<.0001
hs-CRP, mg/L [d]	-0.054 (0.010)	<.0001
Physical activity (MET), h/week	1.23 (0.15)	<.0001
Regular smokers % (n)	-0.0018 (0.0018)	.33
Alcohol consumption (g/day) [d]	-0.0079 (0.013)	.55
Sosio-economic status [c]	0.013 (0.0043)	.0023
Educational level (1-3 mean)	0.026 (0.0052)	<.0001
Projected educational level	0.032 (0.0064)	<.0001

	Female		Male	
	β(SE)[a]	P[b]	β(SE)[a]	P[b]
Insulin, μU/L [d]	-0.020 (0.0051)	<.0001	-0.042 (0.0051)	<.0001
HOMA-IR [d]	-0.021 (0.0058)	.0005	-0.044 (0.0054)	<.0001
hs-CRP, mg/L [d]	-0.082 (0.015)	<.0001	-0.031 (0.012)	.0105

Females and males were analysed seperately for measurements in which value for sex-interaction were $P < 0.05$

Descriptive data: BP, blood pressure; LDL, Low Density Lipoprotein; HDL, High Density Lipoprotein; hs-CRP, high-sensitivity C-reactive protein; MET,

[a] *Regression coefficient (β) and SE for a 1-unit change in fitness; linear regression analysis adjusted for sex.*

[b] *Probability values: regression analyses where fitness is used as a continuous variable.*

[c] *Family income and parent level of education in equally weighted index.*

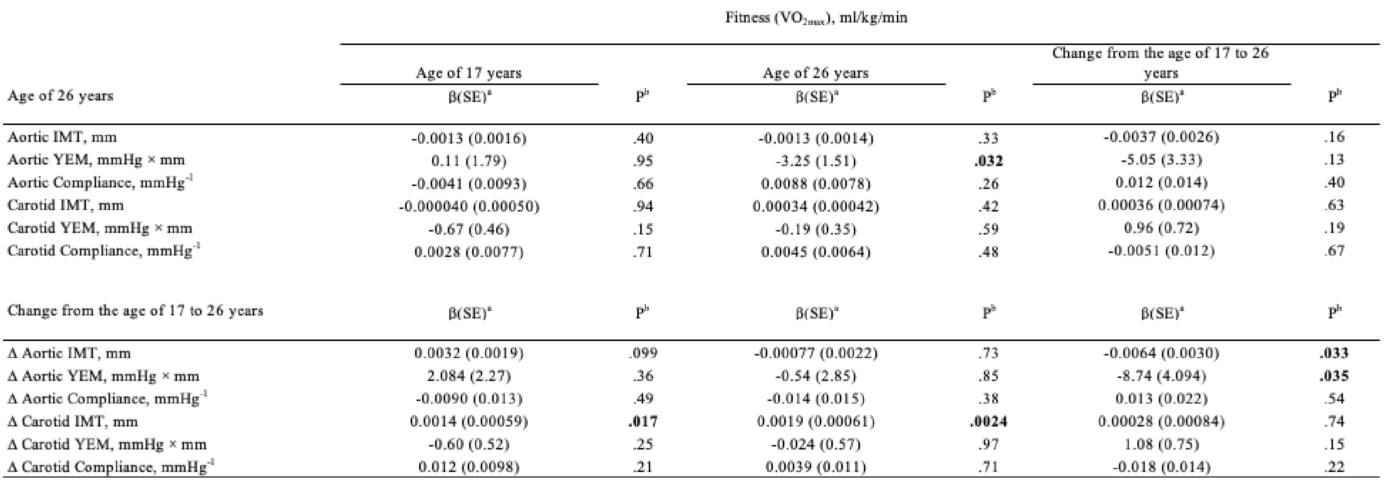
[d] *Logarithmically transformed*

Association of Fitness with Vascular IMT and Elasticity

Table 3 describes the associations of fitness at the age of 17 years, age of 26 years, and the nine-year change in fitness (from the age of 17 to 26 years) with vascular outcomes at the age of 26 years. In addition to cross-sectional measures, the table also illustrates associations of fitness (as described above) with longitudinal changes in vascular (aortic and carotid) IMT, elasticity, and compliance from the age of 17 to 26 years. All analyzes are adjusted for sex.

Fitness at the age of 26 years (treated as a continuous variable) was inversely associated with aortic YEM at the age of 26 years. This favorable association did not remain after adjusting for sex, STRIP intervention/control group, BMI, diastolic blood pressure, total cholesterol, triglycerides, LTPA, insulin, hs-CRP, SES-index and projected educational level. Fitness at the age of 26 years was not associated with any of the other markers of vascular health presented in Table 3, at the age of 26 years.

TABLE 3 Sex-adjusted associations of fitness with vascular intima-media thickness (IMT) and elasticity indices at the age of 26 years, and their longitudinal changes from the age of 17 to 26 years.



	Fitness (VO_{2max}), ml/kg/min					
	Age of 17 years		Age of 26 years		Change from the age of 17 to 26 years	
Age of 26 years	β(SE)[a]	P[b]	β(SE)[a]	P[b]	β(SE)[a]	P[b]
Aortic IMT, mm	-0.0013 (0.0016)	.40	-0.0013 (0.0014)	.33	-0.0037 (0.0026)	.16
Aortic YEM, mmHg × mm	0.11 (1.79)	.95	-3.25 (1.51)	**.032**	-5.05 (3.33)	.13
Aortic Compliance, $mmHg^{-1}$	-0.0041 (0.0093)	.66	0.0088 (0.0078)	.26	0.012 (0.014)	.40
Carotid IMT, mm	-0.000040 (0.00050)	.94	0.00034 (0.00042)	.42	0.00036 (0.00074)	.63
Carotid YEM, mmHg × mm	-0.67 (0.46)	.15	-0.19 (0.35)	.59	0.96 (0.72)	.19
Carotid Compliance, $mmHg^{-1}$	0.0028 (0.0077)	.71	0.0045 (0.0064)	.48	-0.0051 (0.012)	.67
Change from the age of 17 to 26 years	β(SE)[a]	P[b]	β(SE)[a]	P[b]	β(SE)[a]	P[b]
Δ Aortic IMT, mm	0.0032 (0.0019)	.099	-0.00077 (0.0022)	.73	-0.0064 (0.0030)	**.033**
Δ Aortic YEM, mmHg × mm	2.084 (2.27)	.36	-0.54 (2.85)	.85	-8.74 (4.094)	**.035**
Δ Aortic Compliance, $mmHg^{-1}$	-0.0090 (0.013)	.49	-0.014 (0.015)	.38	0.013 (0.022)	.54
Δ Carotid IMT, mm	0.0014 (0.00059)	**.017**	0.0019 (0.00061)	**.0024**	0.00028 (0.00084)	.74
Δ Carotid YEM, mmHg × mm	-0.60 (0.52)	.25	-0.024 (0.57)	.97	1.08 (0.75)	.15
Δ Carotid Compliance, $mmHg^{-1}$	0.012 (0.0098)	.21	0.0039 (0.011)	.71	-0.018 (0.014)	.22

Descriptive data: Bolded values indicate statistical significance (P< .05). YEM, Young's elastic modulus; IMT, intima-media thickness; Δ, change from the age of 17 to 26 years.

[a] *Regression coefficient (β) and SE for a 1-unit change in fitness; linear regression analysis adjusted for sex.*

[b] *Probability values: regression analyses where fitness is used as a continuous variable.*

Fitness at the age of 26 years was directly associated with the change in carotid IMT over time from the age of 17 to 26 years. The association remained after adjusting for common cardiometabolic risk factors (BMI, diastolic blood pressure, total cholesterol, triglycerides, LTPA, insulin), STRIP intervention/control group, hs-CRP, SES-index and projected educational level (β=0.0032, P = .012). There were no associations between fitness at the age of 26 years and the change of other markers of vascular health.

Fitness at the age of 17 years was not associated with any of the markers of vascular health measured at the age of 26 years. However, fitness at the age of 17 years was directly associated with the change of carotid IMT over time (from the age of 17 to 26 years), when adjusted with sex. The association did not remain after adjusting for sex, STRIP intervention/control group, BMI, diastolic blood pressure, total cholesterol, triglycerides, LTPA, insulin, hs-CRP, SES-index and projected educational level. There were no associations between fitness at the age of 17 years and other markers of vascular health at the age of 26 years or change over time from the age of 17 to 26 years.

Association of Change in Fitness Over Time with Vascular IMT and Elasticity

Change in fitness from the age of 17 to 26 years was not associated with any of the markers of vascular health at the age of 26 years when adjusted with sex. In contrast, change in fitness was directly associated with the change in aortic IMT and aortic YEM over time (from the age of 17 to 26 years), adjusted with sex. The association did not remain after adjusting for sex, STRIP intervention/control group, BMI, diastolic blood pressure, total cholesterol, triglycerides, LTPA, insulin, hs-CRP, SES-index and projected educational level. Change in fitness was not associated with change of the other markers of vascular health.

Association of Fitness and Fatty Liver

Associations between fitness and fatty liver at the age of 17 and 26 years are shown in Table 4. As shown in the table, in models adjusted for sex, fitness the age of 17 and 26 years were associated with a lower prevalence of fatty liver at the age of 26 years.

When the analysis was further adjusted for sex, BMI and STRIP study group, the longitudinal association remained significant, with higher fitness at age 17 predicting a lower risk of fatty liver in adulthood. The cross-sectional association between fitness and fatty liver at the age of 26 years followed a similar trend but reached borderline significance after full adjustment. Notably, the vast majority of fatty liver cases were clustered within the lowest fitness tertile. Specifically, all 16 fatty liver cases related to age 17 fitness measurements and 12 out of 14 cases related to age 26 fitness measurements were found in the lowest fitness group.

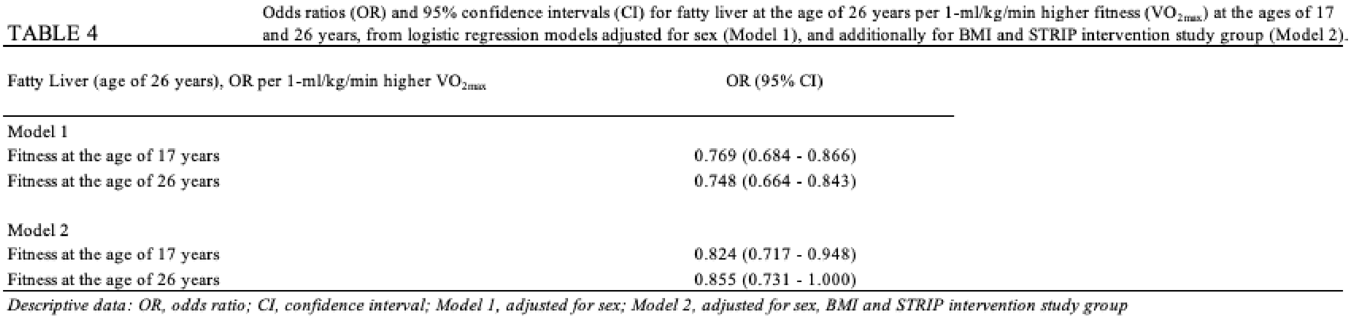


TABLE 4 Odds ratios (OR) and 95% confidence intervals (CI) for fatty liver at the age of 26 years per 1-ml/kg/min higher fitness (VO_{2max}) at the ages of 17 and 26 years, from logistic regression models adjusted for sex (Model 1), and additionally for BMI and STRIP intervention study group (Model 2).

Fatty Liver (age of 26 years), OR per 1-ml/kg/min higher VO_{2max}	OR (95% CI)
Model 1	
Fitness at the age of 17 years	0.769 (0.684 - 0.866)
Fitness at the age of 26 years	0.748 (0.664 - 0.843)
Model 2	
Fitness at the age of 17 years	0.824 (0.717 - 0.948)
Fitness at the age of 26 years	0.855 (0.731 - 1.000)

Descriptive data: OR, odds ratio; CI, confidence interval; Model 1, adjusted for sex; Model 2, adjusted for sex, BMI and STRIP intervention study group

DISCUSSION

Principal Findings

The present study investigated the association of fitness with markers of vascular health and fatty liver in young adults, extending the follow-up of the study population from adolescence to age 26. Our results indicate that the favorable association between fitness and vascular structure, as previously observed at the age of 17 years, does not necessarily persist into young adulthood. While fitness at the age of 26 years was associated with better aortic elasticity in the cross-sectional analysis, this relationship was diluted after adjusting for common cardiometabolic risk factors. This suggests that the association is not independent of the participants overall cardiometabolic risk profile. Interestingly, we found that fitness at the age of 26 years was associated with thickening of carotid IMT over nine-year follow-up. This association remained significant even after full adjustment for risk factors. Furthermore, participants in the STRIP intervention group had a higher cardiorespiratory fitness level at the age of 26 years compared to the control group. This finding is noteworthy, as no such association between the STRIP study groups was detected at the age of 17 years.[23]

Notably, fitness demonstrated a robust and independent association with liver health. Low fitness at the age of 17 and 26 years was a strong predictor of fatty liver prevalence at the age of 26 years, with the vast majority of cases clustered within the lowest fitness tertile. The longitudinal association remained significant, and the cross-sectional association reached a borderline significance, even after adjusting for BMI and STRIP study group. This finding underscores the clinical significance of cardiorespiratory fitness in the early prevention of metabolic liver disease, suggesting that fitness may provide metabolic protection that is independent of overall adiposity.

Fitness and STRIP Study Group

Interestingly, we found that fitness was associated with the STRIP study group at the age of 26 years. This observation contrasts with our previous report at the age of 17 years, where no such association was found.[23] This is likely because physical activity was encouraged but not a structured or continuous part of the intervention. However, the long-term individualized counseling which continued from infancy until the age of 20 years, may have had a latent effect on lifestyle choices that only became evident in young adulthood. It is possible that the sustained dietary education provided to the intervention group fostered an overall increase in health awareness. This may have led to a broader improvement in health behaviors beyond the primary dietary and antismoking targets, such as more regular aerobic exercise or healthier sleep patterns. Furthermore, the transition from adolescence to young adulthood is a critical period for the stabilization of lifestyle routines.[22] While the structured environments of adolescence (e.g., school physical education and organized sports) may have initially masked the subtle effects of the intervention, the differences in health motivation between the groups likely became more pronounced as individuals assumed full responsibility for their personal health by the age of 26 years. These results highlight the potential for early-life lifestyle interventions to provide cumulative benefits that support the maintenance of cardiorespiratory health throughout the transition into independent adulthood.

Fitness and Vascular Adaptation

Our findings highlight distinct differences between the aortic and carotid artery responses to fitness. While in the cross-sectional analysis at the age of 26 years, fitness was favorably associated with aortic elasticity, when adjusted for sex, no such favorable association was observed in the carotid artery. This finding is in line with earlier report from the STRIP study, in which the effects of fitness and physical activity were more pronounced in the abdominal aorta than in the carotid artery during adolescence.[23] The aorta, as a large elastic artery, may be more sensitive in capturing the vascular impacts of fitness in early life, whereas carotid changes might manifest more clearly later in adulthood.[24,45,46]

Intriguingly, the observed association between fitness at the age of 26 years and the nine-year increase in carotid IMT presents a seemingly paradoxical finding. We suggest that this observation reflects physiological remodeling, often referred to as the 'athlete’s artery', rather than early-stage atherosclerosis.[47–49] Crucially, this structural thickening was not accompanied by a simultaneous decrease in arterial elasticity, which typically characterizes pathological vascular aging.[12] Instead, regular and intensive training induces transient elevations in systolic blood pressure and increased wall shear stress during exercise sessions.[49–51] These hemodynamic forces, combined with an increased fat-free mass, likely trigger a non-pathological, compensatory hypertrophy of the carotid wall to accommodate higher metabolic demands.[48,49,51] While evidence on specific carotid adaptation remains heterogeneous, our findings support the view that in fit young adults, a thicker carotid IMT can represent a benign structural adaptation to a chronic exercise loading.

The predictive value of adolescent fitness for vascular changes diminished over time. While clear associations were observed in the initial cross-sectional study at the age of 17 years,[23] these did not persist into early adulthood. Specifically, fitness at the age of 17 years did not predict vascular markers at the age of 26 years, and no significant cross-sectional associations were observed at the 26-year follow-up. Several interrelated mechanisms may explain this attenuated association. Fitness and lifestyle often undergo significant changes during the transition from adolescence to young adulthood.[22,52,53] Furthermore, the cumulative impact of traditional risk factors such as BMI, lipid profiles, and blood pressure may eventually override the initial protective effects of adolescent fitness.[54–56] This process is likely compounded by the natural anatomical thickening of the vascular intima-media during the third decade of life, which may mask the subtle structural benefits gained earlier.[57,58] Together, these results underscore that while adolescent fitness is crucial for early health, maintaining high fitness throughout the transition into adulthood is likely more critical for sustained vascular benefits.

Fitness and Fatty Liver

A key finding of our study is the robust longitudinal association between cardiorespiratory fitness in adolescence and the prevalence of fatty liver in young adulthood. Notably, we observed a heavy clustering of fatty liver cases within the lowest fitness tertile, both longitudinally and cross-sectionally. In the longitudinal analysis, all 16 participants diagnosed with fatty liver at the age of 26 years had been in the lowest fitness tertile at the age of 17 years. This pattern persisted in the cross-sectional analysis at the age of 26 years, where 12 out of 14 detected cases were similarly found in the lowest fitness group. These findings suggest a potential threshold effect, where even a moderate level of cardiorespiratory fitness during the transition to adulthood may serve as a significant protective buffer against hepatic steatosis.

The robust nature of this relationship is further supported by regression models. Fitness at the age of 17 remained a significant predictor of fatty liver at the age of 26 years, even after adjusting for sex, BMI, and STRIP study group. While the cross-sectional association at the age of 26 years reached only a borderline significance after full adjustments, the consistent clustering of cases emphasizes that low fitness remains a relevant clinical marker for liver health.

These results underscore the clinical importance of early-life physical activity interventions and contribute to the "fitness-fatness" discussion by suggesting that the metabolic benefits of fitness on liver health are partially independent of overall adiposity.[28,59,60] The fact that the longitudinal association remained significant after adjusting for BMI indicates that fitness is not merely a surrogate for body weight, but a distinct physiological factor influencing intrahepatic fat accumulation.[29,60] Given that, the transition from adolescence to young adulthood is often marked by changes in lifestyle and a decline in relative cardiorespiratory fitness, our findings highlight low fitness as a major risk factor for metabolic-associated fatty liver disease (MASLD). Consequently, this emphasizes the need for sustained physical activity from adolescence into young adulthood to ensure long-term metabolic health benefits.

Strengths and Limitations

The primary strength of this study is its prospective, longitudinal design within the STRIP project, which allowed for the tracking of cardiorespiratory fitness, vascular health and metabolic risk factors from the age of 17 to 26 years.[30,31] A significant methodological advantage is the use of an objective, maximal cycle ergometer exercise test, providing a reliable measure of cardiorespiratory fitness (VO2max).[17,36,60] In this instance the objective measure of cardiorespiratory fitness is more adequate marker of physical condition than more commonly used, self-reported, LTPA.[35] Furthermore, all vascular measurements were performed using high-quality ultrasonography according to standardized protocols and performed by a trained sonographer. The availability of comprehensive data on cardiometabolic risk factors enabled robust multivariate adjustments to isolate the independent effects of fitness. While the longitudinal sample size (n=136 to 156) may be smaller than in large population-based surveys, the clinical depth provided by objective, maximal cycle ergometer testing and high-quality vascular imaging offers a level of evidence that surpasses larger studies relying on self-reported data.

However, limitations must be acknowledged. The presence of fatty liver was determined visually by ultrasonography rather than through the clinical gold standard of a liver biopsy or magnetic resonance spectroscopy.[42,60] While ultrasound is a practical tool for epidemiological studies, it may be less sensitive in detecting minor degrees of steatosis.[61] Additionally, there was a notable reduction in the number of participants available for analysis at the age of 26 years compared to age of 17 years. Unfortunately, this is a common challenge in long-term follow-up studies that can impact statistical power. Furthermore, the study population consisted of participants in a long-term dietary intervention trial, which may limit the generalizability of the findings to the broader population, even though the intervention group was accounted for in statistical models. Finally, despite adjusting for a wide range of cardiometabolic and lifestyle factors, the influence of unmeasured variables such as genetic predispositions or specific dietary patterns beyond the intervention, cannot be completely excluded.

Conclusions

Our findings demonstrate that fitness is a robust and independent protector against fatty liver during the transition from adolescence to young adulthood. Maintaining at least a moderate level of fitness appears to provide significant protection against early metabolic liver disease. While the favorable associations between fitness and vascular structure observed in adolescence appear to diminish or evolve into physiological remodeling by the age of 26 years, the metabolic benefits of fitness remain distinct and clinically significant. In addition, the observation that the STRIP intervention group had higher fitness levels in young adulthood highlights the potential for long-term, early-life counseling to provide latent benefits for cardiorespiratory and cardiometabolic health. Collectively, these results emphasize that promoting and sustaining cardiorespiratory fitness from youth through the third decade of life is a vital strategy for long-term cardiometabolic risk prevention.

References

1. Ference, B. A. *et al.* Low-density lipoproteins cause atherosclerotic cardiovascular disease. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. *Eur. Heart J.* **38**, 2459–2472 (2017).
2. Jacobs, D. R. *et al.* Childhood Cardiovascular Risk Factors and Adult Cardiovascular Events. *N. Engl. J. Med.* **386**, 1877–1888 (2022).
3. Raitakari, O., Pahkala, K. & Magnussen, C. G. Prevention of atherosclerosis from childhood. *Nat. Rev. Cardiol.* **19**, 543–554 (2022).
4. Choudhury, R. P., Fuster, V. & Fayad, Z. A. Molecular, cellular and functional imaging of atherothrombosis. *Nat. Rev. Drug Discov.* **3**, 913–925 (2004).
5. Olsen, M. H. *et al.* A call to action and a lifecourse strategy to address the global burden of raised blood pressure on current and future generations: the Lancet Commission on hypertension. *The Lancet* **388**, 2665–2712 (2016).
6. Pollock, B. D. *et al.* Life course trajectories of cardiovascular risk: Impact on atherosclerotic and metabolic indicators. *Atherosclerosis* **280**, 21–27 (2019).
7. Pignoli, P., Tremoli, E., Poli, A., Oreste, P. & Paoletti, R. Intimal plus medial thickness of the arterial wall: a direct measurement with ultrasound imaging. *Circulation* **74**, 1399–1406 (1986).
8. Lorenz, M. W., Markus, H. S., Bots, M. L., Rosvall, M. & Sitzer, M. Prediction of Clinical Cardiovascular Events With Carotid Intima-Media Thickness: A Systematic Review and Meta-Analysis. *Circulation* **115**, 459–467 (2007).
9. Dawson, J. D., Sonka, M., Blecha, M. B., Lin, W. & Davis, P. H. Risk Factors Associated With Aortic and Carotid Intima-Media Thickness in Adolescents and Young Adults. *J. Am. Coll. Cardiol.* **53**, 2273–2279 (2009).
10. Mitra, S. *et al.* Carotid intima-media thickness, cardiovascular disease, and risk factors in 29,000 UK Biobank adults. *Am. J. Prev. Cardiol.* **22**, 101011 (2025).
11. Murakami, S. *et al.* Common carotid intima-media thickness is predictive of all-cause and cardiovascular mortality in elderly community-dwelling people: Longitudinal Investigation for the Longevity and Aging in Hokkaido County (LILAC) study. *Biomed. Pharmacother.* **59**, S49–S53 (2005).

12. Vlachopoulos, C., Aznaouridis, K. & Stefanadis, C. Prediction of Cardiovascular Events and All-Cause Mortality With Arterial Stiffness. *J. Am. Coll. Cardiol.* **55**, 1318–1327 (2010).
13. Bots, M. L., Hoes, A. W., Koudstaal, P. J., Hofman, A. & Grobbee, D. E. Common Carotid Intima-Media Thickness and Risk of Stroke and Myocardial Infarction: The Rotterdam Study. *Circulation* **96**, 1432–1437 (1997).
14. O'Leary, D. H. *et al.* Carotid-Artery Intima and Media Thickness as a Risk Factor for Myocardial Infarction and Stroke in Older Adults. *N. Engl. J. Med.* **340**, 14–22 (1999).
15. Singh, B. *et al.* Comparison of objectively measured and estimated cardiorespiratory fitness to predict all-cause and cardiovascular disease mortality in adults: A systematic review and meta-analysis of 42 studies representing 35 cohorts and 3.8 million observations. *J. Sport Health Sci.* **14**, 100986 (2025).
16. Lang, J. J. *et al.* Cardiorespiratory fitness is a strong and consistent predictor of morbidity and mortality among adults: an overview of meta-analyses representing over 20.9 million observations from 199 unique cohort studies. *Br. J. Sports Med.* **58**, 556–566 (2024).
17. Raghuveer, G. *et al.* Cardiorespiratory Fitness in Youth: An Important Marker of Health: A Scientific Statement From the American Heart Association. *Circulation* **142**, (2020).
18. Ross, R., Arena, R., Myers, J., Kokkinos, P. & Kaminsky, L. A. Update to the 2016 American Heart Association cardiorespiratory fitness statement. *Prog. Cardiovasc. Dis.* **83**, 10–15 (2024).
19. Bouchard, C. *et al.* Familial resemblance for ??VO2max in the sedentary state: the HERITAGE family study: *Med. Amp Sci. Sports Amp Exerc.* **30**, 252–258 (1998).
20. Bouchard, C. & Rankinen, T. Individual differences in response to regular physical activity: *Med. Sci. Sports Exerc.* **33**, S446–S451 (2001).
21. Katzmarzyk, P. T., Malina, R. M., Song, T. M. K. & Bouchard, C. Physical activity and health-related fitness in youth: amultivariate analysis: *Med. Sci. Sports Exerc.* **30**, 709–714 (1998).
22. Fraser, B. J. *et al.* Tracking of Cardiorespiratory Fitness and Physical Activity from Youth to Young Adulthood: Findings from the Prospective Special Turku Coronary Risk Factor Intervention Project (STRIP). *J. Pediatr. X* **9**, 100085 (2023).
23. Pahkala, K. *et al.* Association of Fitness With Vascular Intima-Media Thickness and Elasticity in Adolescence. *Pediatrics* **132**, e77–e84 (2013).

24. McGill, H. C. *et al.* Effects of coronary heart disease risk factors on atherosclerosis of selected regions of the aorta and right coronary artery. PDAY Research Group. Pathobiological Determinants of Atherosclerosis in Youth. *Arterioscler. Thromb. Vasc. Biol.* **20**, 836–845 (2000).
25. Green, D. J., Spence, A., Rowley, N., Thijssen, D. H. J. & Naylor, L. H. Vascular adaptation in athletes: is there an 'athlete's artery'? *Exp. Physiol.* **97**, 295–304 (2012).
26. Nugroho, M. I. A. & Rimbun, R. Structural and Functional Adaptations of Blood Vessels to Running: A Literature Review. *Int. J. Sci. Adv.* https://doi.org/10.51542/ijscia.v6i6.33 (2025) doi:10.51542/ijscia.v6i6.33.
27. Rinella, M. E. *et al.* A multisociety Delphi consensus statement on new fatty liver disease nomenclature. *Hepatology* **78**, 1966–1986 (2023).
28. Pälve, K. S. *et al.* Cardiorespiratory Fitness and Risk of Fatty Liver: The Young Finns Study. *Med. Sci. Sports Exerc.* **49**, 1834–1841 (2017).
29. Kantartzis, K. *et al.* High cardiorespiratory fitness is an independent predictor of the reduction in liver fat during a lifestyle intervention in non-alcoholic fatty liver disease. *Gut* **58**, 1281–1288 (2009).
30. Simell, O. *et al.* Cohort Profile: The STRIP Study (Special Turku Coronary Risk Factor Intervention Project), an Infancy-onset Dietary and Life-style Intervention Trial. *Int. J. Epidemiol.* **38**, 650–655 (2009).
31. Pahkala, K. *et al.* Effects of 20-year infancy-onset dietary counselling on cardiometabolic risk factors in the Special Turku Coronary Risk Factor Intervention Project (STRIP): 6-year post-intervention follow-up. *Lancet Child Adolesc. Health* **4**, 359–369 (2020).
32. Kallio, K. *et al.* Decreased Aortic Elasticity in Healthy 11-Year-Old Children Exposed to Tobacco Smoke. *Pediatrics* **123**, e267–e273 (2009).
33. Kallio, K. *et al.* Arterial Intima-Media Thickness, Endothelial Function, and Apolipoproteins in Adolescents Frequently Exposed to Tobacco Smoke. *Circ. Cardiovasc. Qual. Outcomes* **3**, 196–203 (2010).
34. Järvisalo, M. J. *et al.* Increased Aortic Intima-Media Thickness: A Marker of Preclinical Atherosclerosis in High-Risk Children. *Circulation* **104**, 2943–2947 (2001).
35. Pahkala, K. *et al.* Body mass index, fitness and physical activity from childhood through adolescence. *Br. J. Sports Med.* **47**, 71–77 (2013).
36. *ACSM's Guidelines for Exercise Testing and Prescription*. (Lippincott Williams & Wilkins, Philadelphia, 2000).

37. Raitakari, O. T. *et al.* Patterns of intense physical activity among 15- to 30-year-old Finns: The Cardiovascular Risk in Young Finns Study. *Scand. J. Med. Sci. Sports* **6**, 36–39 (1996).
38. Pahkala, K. *et al.* Association of physical activity with vascular endothelial function and intima-media thickness. *Circulation* **124**, 1956–1963 (2011).
39. Mansikkaniemi, K. *et al.* Cross-sectional associations between physical activity and selected coronary heart disease risk factors in young adults. The Cardiovascular Risk in Young Finns Study. *Ann. Med.* **44**, 733–744 (2012).
40. Repo, O. *et al.* Randomized 20-year infancy-onset dietary intervention, life-long cardiovascular risk factors and retinal microvasculature. *Eur. Heart J.* **45**, 3072–3085 (2024).
41. Niinikoski, H. *et al.* Impact of Repeated Dietary Counseling Between Infancy and 14 Years of Age on Dietary Intakes and Serum Lipids and Lipoproteins: The STRIP Study. *Circulation* **116**, 1032–1040 (2007).
42. Edens, M. A. *et al.* Ultrasonography to Quantify Hepatic Fat Content: Validation by 1H Magnetic Resonance Spectroscopy. *Obesity* **17**, 2239–2244 (2009).
43. Suomela, E. *et al.* Childhood predictors of adult fatty liver. The Cardiovascular Risk in Young Finns Study. *J. Hepatol.* **65**, 784–790 (2016).
44. Saverymuttu, S. H., Joseph, A. E. & Maxwell, J. D. Ultrasound scanning in the detection of hepatic fibrosis and steatosis. *BMJ* **292**, 13–15 (1986).
45. Königstein, K. *et al.* Exercise and Carotid Properties in the Young–The KiGGS-2 Study. *Front. Cardiovasc. Med.* **8**, 767025 (2022).
46. Bia, D. *et al.* [Regional differences in viscosity, elasticity and wall buffering function in systemic arteries: pulse wave analysis of the arterial pressure-diameter relationship]. *Rev. Esp. Cardiol.* **58**, 167–174 (2005).
47. Baumgartner, L., Weberruß, H., Engl, T., Schulz, T. & Oberhoffer-Fritz, R. Exercise Training Duration and Intensity Are Associated With Thicker Carotid Intima-Media Thickness but Improved Arterial Elasticity in Active Children and Adolescents. *Front. Cardiovasc. Med.* **8**, 618294 (2021).
48. Baumgartner, L. *et al.* Improved Carotid Elasticity but Altered Central Hemodynamics and Carotid Structure in Young Athletes. *Front. Sports Act. Living* **3**, 633873 (2021).
49. Böhm, B. & Oberhoffer, R. Vascular health determinants in children. *Cardiovasc. Diagn. Ther.* **9**, S269–S280 (2019).

50. Green, D. J., Hopman, M. T. E., Padilla, J., Laughlin, M. H. & Thijssen, D. H. J. Vascular Adaptation to Exercise in Humans: Role of Hemodynamic Stimuli. *Physiol. Rev.* **97**, 495–528 (2017).
51. Winder, B. *et al.* The association of physical activity and carotid intima-media-thickness in adolescents—data of the prospective early vascular ageing-tyrol cohort study. *Front. Pediatr.* **13**, 1527132 (2025).
52. Winpenny, E. M. *et al.* Changes in diet through adolescence and early adulthood: longitudinal trajectories and association with key life transitions. *Int. J. Behav. Nutr. Phys. Act.* **15**, 86 (2018).
53. Werneck, A. O. *et al.* Cohabitation and marriage during the transition between adolescence and emerging adulthood: A systematic review of changes in weight-related outcomes, diet and physical activity. *Prev. Med. Rep.* **20**, 101261 (2020).
54. Juonala, M. *et al.* Life-time risk factors and progression of carotid atherosclerosis in young adults: the Cardiovascular Risk in Young Finns study. *Eur. Heart J.* **31**, 1745–1751 (2010).
55. Raitakari, O. T. *et al.* Cardiovascular Risk Factors in Childhood and Carotid Artery Intima-Media Thickness in Adulthood: The Cardiovascular Risk in Young Finns Study. *JAMA* **290**, 2277 (2003).
56. Berenson, G. S. *et al.* Association between Multiple Cardiovascular Risk Factors and Atherosclerosis in Children and Young Adults. *N. Engl. J. Med.* **338**, 1650–1656 (1998).
57. Juonala, M. *et al.* Effect of age and sex on carotid intima-media thickness, elasticity and brachial endothelial function in healthy adults: the cardiovascular risk in Young Finns Study. *Eur. Heart J.* **29**, 1198–1206 (2008).
58. Tanaka, H. *et al.* Regular aerobic exercise and the age-related increase in carotid artery intima-media thickness in healthy men. *J. Appl. Physiol.* **92**, 1458–1464 (2002).
59. Jia, Y. *et al.* Independent and joint relationships of cardiorespiratory fitness and body mass index with liver fat content. *Diabetes Obes. Metab.* **26**, 5087–5096 (2024).
60. Zinterl, I. *et al.* Low cardiopulmonary fitness is associated with higher liver fat content and higher GAMMA-GLUTAMYLTRANSFERASE concentrations in the general population – "The Sedentary's Liver". *Liver Int.* **42**, 585–594 (2022).
61. Joy, D., Thava, V. R. & Scott, B. B. Diagnosis of fatty liver disease: is biopsy necessary? *Eur. J. Gastroenterol. Hepatol.* **15**, 539–543 (2003).