International Journal of Cardiology 230 (2017) 304–309

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Ideal cardiovascular health in childhood—Longitudinal associations with cardiac structure and function: The Special Turku Coronary Risk Factor Intervention Project (STRIP) and the Cardiovascular Risk in Young Finns Study (YFS)

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A R T I C L E I N F O

Article history:
Received 29 August 2016
Received in revised form 28 November 2016
Accepted 17 December 2016
Available online 23 December 2016

Keywords:
Left ventricular mass
Risk factors
Diastolic dysfunction
Echocardiography
Cardiovascular disease prevention

A B S T R A C T

Background: Ideal cardiovascular health (CVH), defined by the American Heart Association, is associated with incident cardiovascular disease in adults. However, association of the ideal CVH in childhood with current and future cardiac structure and function has not been studied.

Methods and results: The sample comprised 827 children participating in the longitudinal Special Turku Coronary Risk Factor Intervention Project (STRIP) and The Cardiovascular Risk in Young Finns Study (YFS). In STRIP, complete data on the seven ideal CVH metrics and left ventricular (LV) mass measured with echocardiography were available at the age of 15 ($n = 321$), 17 ($n = 309$) and 19 ($n = 283$) years. In YFS, the cohort comprised children aged 12–18 years ($n = 506$) with complete ideal CVH metrics data from childhood and 25 years later in adulthood, and echocardiography performed in adulthood. In STRIP, ideal CVH score was inversely associated with LV mass during childhood ($P = 0.036$). In YFS, childhood ideal CVH score was inversely associated with LV mass, LV end-diastolic volume, E/e′ ratio, and left atrium end-systolic volume in adulthood (all $P < 0.01$). In addition, improvement of the ideal CVH score between childhood and adulthood was inversely associated with LV mass, LV end-diastolic volume, E/e′ ratio, and left atrium end-systolic volume (all $P \leq 0.03$).

Conclusions: Childhood ideal CVH score has a long-lasting effect on cardiac structure and function, and the association is evident already in childhood. Our findings support targeting the ideal CVH metrics as part of primordial prevention of cardiovascular diseases.

1. Introduction

Cardiovascular diseases (CVD) are largely preventable; unhealthy behaviors such as physical inactivity, smoking, and poor diet raise the risk for CVDs. Extensive evidence has demonstrated that low-risk cardiovascular risk factor profiles are associated with large reductions in cardiovascular morbidity and mortality [1,2]. In 2010, the American Heart Association (AHA) published the first formal definition of

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http://dx.doi.org/10.1016/j.ijcard.2016.12.117
0167-5273/

cardiovascular health (CVH) for children and adults as part of their 2020 impact goals [3]. The metrics used to indicate CVH included 4 health behaviors and 3 health factors. The behavioral criteria were non-smoking, being physically active, having normal body mass index (BMI), and a healthy diet. Normal blood pressure, and serum total cholesterol and glucose levels indicated ideal health factors.

A greater number of CVH metrics in middle age has been associated with lower risk of incident CVD and better cardiovascular structure and function among the elderly [4–6]. Previously, we have reported that higher levels of CVH in childhood and increasing CVH status between childhood and adulthood to be associated with lower risk of subclinical atherosclerosis (coronary calcium, heightened carotid intima-media thickness [IMT], arterial stiffening) in adulthood [7–9]. In addition, we have shown ideal CVH to be beneficially associated with vascular health already in adolescence [10]. Recently, it has been shown that a higher of CVH metrics in young adulthood was associated with lower left ventricular (LV) mass and lower risk for diastolic dysfunction later in life [11].

These data are important as changes in cardiac structure and function have predictive value for early CVD morbidity and mortality [12–14]. However, studies examining the effect of ideal CVH in childhood on cardiac structure and function during childhood and adulthood are lacking. Using data from the longitudinal Special Turku Coronary Risk Factor Intervention Project (STRIP) we examined whether childhood ideal CVH is associated with LV mass in individuals studied repeatedly at the age of 15, 17 and 19 years. Additionally, with data from the Cardiovascular Risk in Young Finns Study (YFS), we studied the long-term effect of ideal CVH in childhood (12–18 years of age) on cardiac structure as well as systolic and diastolic function 25 years later in adulthood. Further, we examined the effect of a favorable change in ideal CVH from childhood to adulthood on these cardiac measures.

2. Methods

The study comprised 827 participants from two longitudinal Finnish cohorts, the STRIP and the YFS. Both studies were approved by local ethics committees and all participants provided written informed consent.

2.1. The Special Turku Coronary Risk Factor Intervention Project (STRIP)

The STRIP study is a prospective, randomized controlled trial which aims to prevent atherosclerosis beginning in infancy [15]. Families of 5-month-old infants were recruited to the study at well-baby clinics in Turku, Finland, between February 1990 and June 1992. At the age of 7 months, 1062 infants were randomized to an intervention group ($n = 540$) or to a control group ($n = 522$). Thereafter, the participants have been closely followed up until age 20 years. During the study visits the intervention group has repeatedly received individualized dietary and lifestyle counseling to reduce exposure of the intervention children to environmental atherosclerosis risk factors [16].

The present sample comprised children who had complete data on the ideal CVH metrics and cardiac ultrasound performed at the age of 15 ($n = 321$), 17 ($n = 309$) and 19 ($n = 283$) years (complete data on all three cardiac ultrasound assessments was not required). Representativeness of the participants in this study was examined by comparing their characteristics at the age of 15 to those who did not have complete ideal CVH and cardiac ultrasound data at the same age. We observed that participants in this study had lower concentrations of total cholesterol and LDL-cholesterol compared to those not included in the study (Supplemental Table 1). No differences were observed in other ideal health factors, serum lipids or ideal health behaviors.

2.2. The Cardiovascular Risk in Young Finns Study (YFS)

The YFS is on ongoing multicenter follow-up study to assess risk factors underlying CVD [17]. The first cross-sectional survey was conducted in 1980, when 3596 individuals aged 3 to 18 years participated. These participants were randomly chosen from the national register of the study areas in different parts of Finland. Since 1980, several follow-up studies have been conducted. The latest 31-year follow-up survey was performed in 2011, when 2063 (aged 34–49 years) of the original participants attended. For the present study, we chose year 1986 as the baseline because it was the first follow-up at which glucose values were measured. In total, the sample comprised 506 children aged 12–18 years that had complete data on ideal CVH metrics in 1986 and 2011, and had undergone cardiac ultrasound examinations in 2011. Representativeness of participants in this study was examined by comparing their baseline characteristics (1986) with those who did not attend or did not have the complete data in the 2011 follow-up. We observed that participants in this study were older and more often female, and they had lower BMI, higher prevalence of ideal diet, and lower prevalence of ideal physical activity compared with those not included in the study. (Supplemental Table 1) No other differences were observed in ideal health factors, serum lipids or ideal smoking status between participants and non-participants.

2.3. Metrics for cardiovascular health

Where possible, we followed the metrics as described by the AHA [3]. Childhood ideal CVH metrics were applied for all STRIP participants and at baseline in the YFS. All cut-off points in the present study are age and sex specific [3]. Adult ideal CVH metrics were applied for YFS participants in 2011.

2.3.1. Health factors

All laboratory measurements were performed using fasting blood samples. Serum cholesterol determinations were performed with standard methods reported previously [15,18]. In children, ideal total cholesterol status was defined as <4.4 mmol/l (<170 mg/dl) and in adults as <5.2 mmol/l (<200 mg/dl). In YFS, blood pressure was measured using a random zero sphygmomanometer. In STRIP, an oscillometric device was used [15]. In children, ideal blood pressure status was defined as systolic blood pressure (SBP) <90th percentile and diastolic blood pressure (DBP) <90th percentile, and in adults as SBP <120 mmHg and DBP <80 mmHg. Fasting plasma glucose concentrations were analyzed enzymatically and classified in children and adults as ideal <5.6 mmol/l (<100 mg/dl) [3].

2.3.2. Health behaviors

Height and weight were measured, and BMI calculated as BMI = weight, kg/(height, m) [2]. In children, ideal BMI was classified as <85th percentile and in adults as <25 kg/m^2 [3]. In YFS, ideal diet score in 1986 was defined as having 2–3 of 3 ideal diet components (fruits and vegetables, fish, soft drinks), as previously described [7]. In the YFS follow-up in 2011 and in STRIP, achievement of the 5 AHA ideal dietary goals (fruits and vegetables, fish, sodium, whole grains, and sugar-sweetened beverages) was categorized as previously described [7,10]. Ideal diet score was defined as having 4–5 of these 5 ideal diet components [3]. Children who reported never to have smoked a cigarette were categorized as having an ideal smoking status. In YFS, adults were classified as current smokers (non-ideal) and never or former smokers (ideal). Physical activity was assessed by questionnaires. The AHA's definition of ideal physical activity in children is ≥60 min of moderate or vigorous activity every day. In YFS, this definition was approximated as ≥7 h of moderate or vigorous activity per week [7]. In STRIP, a criterion of leisure time physical activity >30 metabolic equivalent h/week corresponding to >1 h/day of moderate intensity physical activity was used [10]. In adults, the AHA definition of ideal physical activity (≥-150 min/week moderate or ≥75 min/week vigorous intensity or ≥150 min/weekmoderate + vigorous) was approximated as ≥1 h/.week vigorous or ≥2–3 h/w.eek moderate or ≥2–3 h/week. moderate + vigorous in the present study [7].

2.4. Ideal cardiovascular health score

From the individual health factors and behaviors described above, we generated the corresponding ideal CVH score. To create the score, a value of 1 was assigned for each metric if the criterion for ideal CVH was met. In case the criterion was not met, a value of 0 was assigned. The range of the ideal CVH score was thus 0 to 7, a higher score indicating a better CVH profile. Low CVH was defined as ≤3 metrics and high CVH as ≥4 metrics present [10]. Four CVH groups were formed in YFS cohort; Persistently high group: high CVH in childhood and high CVH in adulthood ($N = 148$); Incident: low CVH in childhood but high CVH in adulthood ($N = 125$); Resolution: high CVH in childhood, but low CVH in adulthood ($N = 115$); and Persistently low: low CVH in childhood and in adulthood ($N = 118$). In addition, we created a separate health behavior score (range 0–4) and a health factor score (range 0–3).

2.5. Echocardiography

The echocardiographic examinations were performed according to the American and European guidelines [19,20]. In both cohorts, transthoracic echocardiograms were performed with Acuson Sequoia 512 (Acuson Mountain View, California, USA) ultrasonography, using a 3.5 MHz scanning frequency phased-array transducer. In both cohorts, analyses of the echo images were performed by a single observer. Both the sonographer and the observer were blinded to the subject's details.

In STRIP, echocardiography was performed at the age of 15, 17, and 19 years successfully in 418, 394, and 420 adolescents, respectively [21]. In STRIP, the following measurements: end-diastolic interventricular septal wall thickness, end-diastolic posterior wall thickness, and end-diastolic LV internal diameter were obtained from the parasternal long axis view in M-mode.

In YFS, echocardiographic data were obtained at the 2011 follow-up on 1680 participants [22]. From these 1680 individuals, 506 were 12–18 years old at baseline (1986) and had complete ideal CVH data available both from baseline and follow-up in 2011 (age 37–43 years). These 506 participants were thus included in the analyses of this study. Standard echocardiographic examinations were produced from the standardized image planes and modes: parasternal long and short axis in 2D and M mode and apical four chamber view [19]. Based on the recommendations to assess LV ejection fraction, the end-diastolic and end-systolic volume were measured from the apical 4-chamber view [19,20]. LV ejection fraction was calculated as follows: Ejection fraction (EF) = 100 × (LV end-diastolic volume-LV end-systolic volume) / LV end-diastolic volume. Transmitral flow and tissue velocities were measured using continuous and pulsed-wave Doppler to define LV diastolic performance index, E/e′-ratio, as previously described [22].

In both cohorts, LV mass was calculated as follows: LV mass = (0.8[1.04(LV end-diastolic diameter + posterior wall thickness + septal wall thickness) [3] − LV end-diastolic diameter) [3]] + 0.6 g [19,21]. Body size was taken into account in the form of current BMI (as part of the ideal CVH score) in all analyses. LV mass was indexed according to height at the allometric power of 2.7 (LV mass index = LV mass / heigh$^{2.7}$) because this indexation may perform best in the context of overweight/obesity [23]. In additional analyses, ventricular and atrial volumes were indexed to body surface area (BSA).

2.6. Statistical analyses

Due to the low prevalence of children with 0 or 1 of the ideal CVH metrics in the STRIP study ($N = 5$), children with 0, 1 and 2 metrics were combined for the analyses in this cohort. Repeated measures linear regression analysis (compound symmetry covariance structure) adjusted for age and sex was used to study the association of the ideal CVH score with LV mass. We have previously reported that the STRIP study group (intervention *vs.* control) is associated with ideal CVH score [10]. In this study, there was no STRIP study group × ideal CVH score interaction when LV mass was the outcome variable, indicating that the effect of the score on LV mass is similar in the STRIP intervention and control groups. Therefore, the STRIP study groups were analyzed combined.

In YFS, to study the associations of childhood ideal CVH score and change in the score (score in 2011 − score in 1986) with cardiac structure and function in adulthood multivariable linear regression models adjusted for baseline score, change in the score, age at baseline, and sex were performed. All statistical tests were performed using SAS version 9.4 (SAS institute, Inc., Cary, NC) with statistical significance inferred at a 2-tailed P-value < 0.05.

3. Results

Characteristics of the STRIP participants at the age of 15 and the YFS participants at the age of 12 to 18 years are shown in Table 1. In the STRIP children, mean LV mass was 108 g in females and 131 g in males. In the YFS participants in adulthood (aged 37 to 43 years) mean LV mass was 114 g in females and 158 g in males. In childhood, participants met on average 4.3 ± 1.1 and 3.6 ± 1.0 of all 7 ideal metrics in STRIP and YFS, respectively.

Age and sex adjusted mean LV mass index in childhood according to the number of ideal cardiovascular health metrics in the STRIP study is shown in Fig. 1. Higher ideal CVH score was associated with lower LV mass index during childhood ($p = 0.004$, Fig. 1). The results were essentially similar when LV mass was used as the outcome variable ($p = 0.036$, Supplemental Fig. 1). There was no age × score or sex × score interaction indicating that the effect of the ideal CVH score on LV mass and LV mass index was similar at ages 15, 17 and 19, and in females and males.

Table 2 shows childhood ideal CVH score in predicting cardiac structure and function 25 years later in adulthood in YFS. Childhood ideal CVH score was inversely associated with LV mass index, LV mass, LV end-diastolic volume, E/e′ ratio, and left atrium (LA) end-systolic volume in adulthood independently of change in ideal CVH score between childhood and adulthood. Mean adult LV mass index according to the number of childhood ideal cardiovascular health metrics is depicted in Fig. 2, showing a lower adult LV mass index ($P = 0.0001$) with higher childhood ideal CVH score. Further, a favorable change in ideal CVH score was inversely associated with LV mass index, LV mass, LV end-diastolic volume, E/e′ ratio, and LA end-systolic volume (Table 2). The associations of childhood ideal CVH score and change in ideal CVH score with LV end-diastolic volume ($P = 0.88$, and $P = 0.66$, respectively) and LA end-systolic volume ($P = 0.28$, and $P = 0.92$, respectively) were attenuated when volumes were indexed to BSA.

Compared with participants with persistently high ideal CVH score (≥ 4 ideal metrics both in childhood and adulthood), those with persistently low score (≤3 ideal metrics both in childhood and adulthood) had higher LV mass ($P = 0.0006$, Supplemental Fig. 2) and higher E/e′ ratio ($P = 0.0009$, Fig. 3) in adulthood. The LV mass or E/e′ ratio of participants who improved their CVH status from low to high (incident group) was not statistically different from those in the persistently high group. The results were similar for LV end-diastolic volume, LA end-systolic volume, and LV mass index (data not shown).

In YFS, we also studied the independent associations of a favorable change (*i.e.* increase) in ideal CVH factor and CVH behavior scores between childhood and adulthood on cardiac structure and function (Table 3). Favorable change in the ideal CVH factor score was inversely associated with LV mass, LV end-diastolic volume, and E/e′ ratio. Association of the change in the CVH factor score with LV ejection fraction was

Table 1
Characteristics and cardiac structure and function in the STRIP ($N = 321$) and YFS ($N = 506$) cohorts.
Data are mean (SD) for continuous variables and percent for dichotomous variables.

	STRIP (in 2004–2006)		YFS (in 1986)	
	Female	Male	Female	Male
N	146	175	295	211
Baseline characteristics				
Age, years	15.0 (0.05)	15.0 (0.04)	15.0 (2.5)	15.1 (2.4)
CVH behaviors				
BMI, kg/m^2	20.8 (3.1)	20.1 (2.9)	20.0 (2.7)	19.9 (2.7)
Ideal diet, %	0.7	0.6	28.1	24.6
Ideal physical activity, %	48.0	56.0	2.7	7.6
Ideal smoking status , %	76.0	67.4	27.5	19.9
CVH factors				
Systolic BP, mmHg	114.6 (11.2)	120.9 (12.1)	112.3 (10.0)	117.4 (13.1)
Diastolic BP, mmHg	61.2 (6.4)	61.7 (7.2)	64.8 (8.6)	64.4 (10.0)
Glucose, mmol/l	4.8 (0.3)	5.0 (0.3)	4.6 (0.9)	4.8 (0.4)
Total cholesterol, mmol/l	4.1 (0.7)	3.7 (0.7)	5.0 (0.9)	4.7 (1.0)
Cardiac structure and function[*]				
LV mass, g	108.4 (21.1)	131.1 (27.5)	114.3 (22.3)	157.5 (33.8)
LV mass index, g/m$^{2.7}$	27.3 (5.4)	29.2 (5.4)	29.0 (5.8)	31.9 (6.7)
LV end-diastolic volume, ml			113.6 (21.1)	152.0 (30.1)
LV end-diastolic volume index, ml/m^2			63.6 (10.4)	73.5 (13.4)
Ejection fraction, %			58.9 (3.5)	57.7 (3.0)
E/e″ ratio			4.9 (1.0)	4.6 (1.0)
LA end-systolic volume, ml			39.1 (11.5)	47.7 (15.3)
LA end-systolic volume index, ml/m^2			21.8 (5.7)	23.0 (6.8)

Abbreviations, STRIP = the Special Turku Coronary Risk Factor Intervention Project, YFS = the Cardiovascular Risk in Young Finns Study, CVH = cardiovascular health, BMI = body mass index, BP = blood pressure, LV = left ventricle, LA = left atrium.
* In STRIP, LV mass was measured in childhood [mean (SD) age 15.0 (0.05) years], in YFS the cardiac measurements were performed in adulthood [mean (SD) age 40.1 (2.4) years].

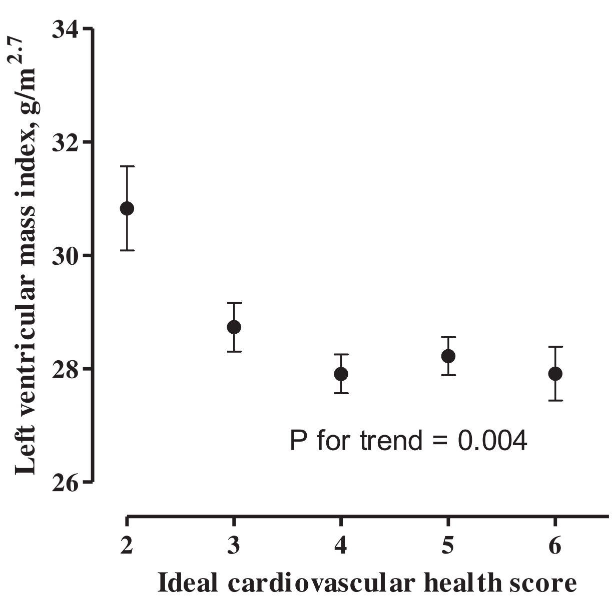

Fig. 1. Means (SE) left ventricular mass index, adjusted for age and sex, according to the number of ideal cardiovascular health metrics in the STRIP study. Children with 0 or 1 ideal metrics are combined with those who have 2 ideal metrics.

Table 2
Childhood ideal cardiovascular health (CVH) and favorable change in CVH between childhood and adulthood in predicting cardiac structure and function in adulthood in the YFS.

	β (SE)	*p*-value
LV mass index, g/m$^{2.7}$ ($N = 489$)		
Childhood CVH	−1.3 (0.3)	0.0001
Favorable CVH change	−1.0 (0.2)	<0.0001
LV mass, g ($N = 489$)		
Childhood CVH	−4.1 (1.5)	0.006
Favorable CVH change	−2.9 (0.9)	0.001
LV end-diastolic volume, ml ($N = 494$)		
Childhood CVH	−3.7 (1.4)	0.006
Favorable CVH change	−2.4 (0.8)	0.004
Ejection fraction, % ($N = 493$)		
Childhood ideal CVH	0.01 (0.18)	0.95
Favorable CVH change	0.05 (0.11)	0.65
E/e′ ratio ($N = 497$)		
Childhood CVH	−0.14 (0.05)	0.006
Favorable CVH change	−0.12 (0.03)	0.0001
LA end-systolic volume , ml ($N = 491$)		
Childhood CVH	−2.0 (0.7)	0.005
Favorable CVH change	−1.0 (0.4)	0.03

Regression coefficients for a 1 unit increase in childhood ideal CVH score and ideal CVH change, both included in the same model. Additionally, age at baseline and sex are included in the model. LV = Left ventricle, LA = Left atrium.

different in males and females [sex × change in CVH factor score interaction: $P = 0.049$]. Favorable change in CVH factor score was inversely associated with LV ejection fraction in males, but not in females. In addition, favorable change in the ideal CVH factor score was inversely associated with LV mass index (β = −1.0, SE = 0.3, $p = 0.0005$). For the ideal CVH behavior score, a favorable change in it was inversely associated with E/e′ ratio. Association of change in the CVH behavior score with LA end-systolic volume was different in males and females [sex × change in CVH behavior score interaction: $P = 0.004$]. Favorable change in CVH behavior score was inversely associated with LA end-systolic volume in females, but not in males. The association of change in the CVH behavior score with LV mass was borderline significant, while a favorable change in the score was inversely associated with LV mass index (β = −1.1, SE = 0.3, $p = 0.0003$).

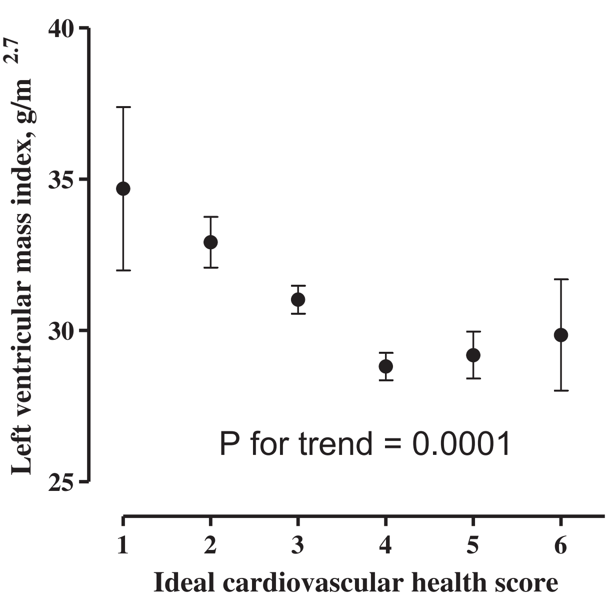

Fig. 2. Mean (SE) left ventricular mass index, adjusted for age, sex and change in ideal cardiovascular health score between childhood and adulthood, according to the number of ideal cardiovascular health metrics in the Cardiovascular Risk in Young Finns Study.

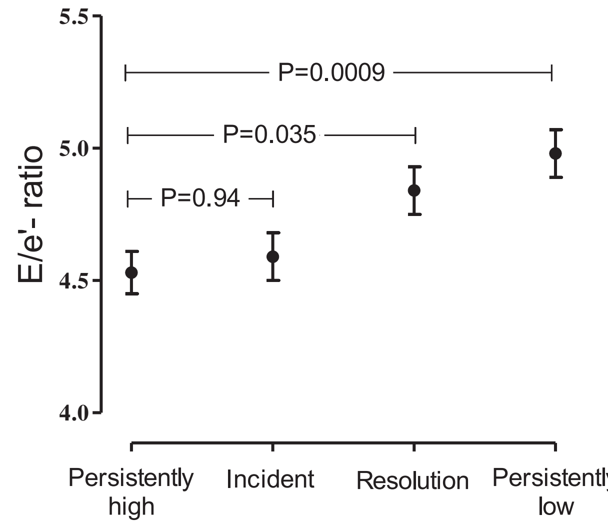

Fig. 3. Age and sex adjusted mean (SE) adult E/e′ ratio according to ideal cardiovascular health status in childhood and adulthood in the Cardiovascular Risk in Young Finns Study. Persistently high group: high CVH (≥4 metrics) in childhood and high CVH in adulthood ($N = 145$); Incident: low CVH (≤3 metrics) in childhood but high CVH in adulthood ($N = 125$); Resolution: high CVH in childhood, but low CVH in adulthood ($N = 111$); and Persistently low: low CVH in childhood and in adulthood ($N = 116$).

4. Discussion

In this study, we applied the AHA 2020 impact goal metrics to two established long-term prospective studies of CVH in children. To the best of our knowledge, this is the first study to investigate the relationship of ideal CVH in childhood with echo measures of cardiac structure and function in both childhood and in later life. We observed that the ideal CVH score in childhood is favorably associated with LV mass already at this young age. The association of childhood ideal CVH score on cardiac structure and function was long-lasting; children with greater ideal CVH score had also better measures of cardiac structure and function almost three decades later in adulthood. In addition, a favorable change in ideal CVH during the life-course was associated with better cardiac structure and function in adulthood.

Table 3
Favorable change in the ideal cardiovascular health (CVH) factor and behavior scores between childhood and adulthood in predicting cardiac structure and function in adulthood in the YFS.

	β (SE)	*p*-value
LV mass, g ($N = 489$)		
Change in ideal CVH factors	−3.3 (1.3)	0.01
Change in CVH behaviors	−2.4 (1.3)	0.06
LV end-diastolic volume, ml ($N = 494$)		
Change in ideal CVH factors	−2.9 (1.2)	0.017
Change in CVH behaviors	−1.9 (1.2)	0.11
Ejection fraction, % ($N = 493$)		
Change in ideal CVH factors*	0.12 (0.16)	0.44
Change in CVH behaviors	−0.02 (0.16)	0.88
E/e′ ratio ($N = 497$)		
Change in ideal CVH factors	−0.14 (0.05)	0.002
Change in CVH behaviors	−0.10 (0.05)	0.03
LA end-systolic volume , ml ($N = 491$)		
Change in ideal CVH factors	−1.1 (0.6)	0.09
Change in CVH behaviors**	−0.8 (0.6)	0.18

Regression coefficients are for a 1 unit increase in the change in ideal CVH factor score and change in ideal CVH behavior score, both included in the same model. Additionally, age at baseline and sex are included in the model. LV = Left ventricle, LA = Left atrium.

* Significant sex interaction; males: β (SE) = 0.49 [0.21], $p = 0.02$, females: β (SE) = −0.22 (0.24), $p = 0.36$.

** Significant sex interaction; males β (SE) = 1.4 [1.1], $p = 0.23$, females: β (SE) = −2.4 (0.7), $p = 0.0007$.

LV hypertrophy is strong predictor of CVD morbidity in adulthood [12,13]. Two previous studies in middle aged adults have shown that a greater number of CVH metrics is associated with better cardiovascular structure and function among the elderly [5,6]. In a recent report, a higher number of CVH metrics in young adulthood was associated with lower LV mass and lower risk for diastolic dysfunction later in life [11]. In line with the results observed in adults, we found that the AHA ideal CVH score for children predicted lower LV mass already in childhood and moreover later in adulthood. Moreover, our data showed that individuals who improve their CVH by some means between childhood and adulthood to have similar levels of cardiac structure and function to those who had high CVH scores in both childhood and adulthood. These results suggest not only the pursuit of ideal CVH already in childhood to be important to prevent unfavorable cardiac growth, but that those children with low CVH are not destined to maintain this risk, if their CVH can be improved.

We have previously reported that ideal CVH in childhood and a favorable change in ideal CVH status is associated with lower risk of coronary artery calcification, high-risk carotid IMT and arterial stiffness [7–9]. Here we observed that persons with persistently low CVH status in childhood and adulthood had higher LV mass, higher LV end-diastolic volume, higher end-systolic left atrial volume and poorer LV diastolic function in adulthood. However, those persons who improved their ideal CVH score from low to high had similar measures of cardiac structure and function in adulthood compared with those who had high CVH scores at both time points. Interestingly, we also found that improvement in ideal CVH factor score between childhood and adulthood was associated with better LV ejection fraction, an important measure of LV systolic function, in males. Results of this study mirror our previous reports showing that childhood overweight-related risks for type 2 diabetes, hypertension, high risk IMT and dyslipidemia are reversible among those individuals who become non-obese adults [24] and that metabolic syndrome in youth that resolves by adult life is associated with a normalization of type 2 diabetes [25]. Collectively, these data suggest that although only few, on average, of the ideal CVH metrics were met in childhood, improvement in CVH status is reflected by cardiac structure and function consistent with better CVH in later life. These data give a positive message to health care providers encouraging children and young adults in lifestyle improvement.

LV diastolic function is recognized as an important marker of hemodynamic status and diastolic dysfunction is prognostic of incident heart failure [14]. LA enlargement associates with decreased diastolic function [26] and it is an early marker for CVD outcomes, such as atrial fibrillation, thrombus formation and sudden death [27]. Here, we examined LV diastolic function by using the ratio of E to e′, where E wave in the pulsed Doppler registration describes the early mitral inflow in diastole, and e′ in the tissue Doppler registration measures the mitral annular longitudinal velocity, calculated as a mean of lateral and septal velocities, in early diastole. The ratio of E to e′ is considered the best echocardiographic measurement of diastolic function in the estimation of LV filling pressure [20]. In this study, we observed that children with higher ideal CVH score had better LV diastolic function—both LV filling pressure (E/e′) and LA end-diastolic volume—in adulthood. We also found that improvement in the CVH behavior score between childhood and adulthood, independent of change in the CVH factors, predicted better diastolic function. This finding is clinically important, because it highlights the importance of improving health behaviors as opposed to only controlling individual health factors with medication.

This study had limitations. Firstly, cardiac magnetic resonance imaging may be a more sensitive way to measure LV mass and volumes than transthoracic echocardiography. However, echocardiography is still the most used application particularly in clinical practice. In addition, apical two-chamber view was not obtained in this study, and thus we were not able to assess LV ejection fraction with the biplane method of disks, which is the recommended method of choice [19]. Secondly, even though measurement of major risk factors is well standardized and therefore relatively generalizable from study to study, measurement of diet and physical activity is not. In STRIP, data on diet was obtained using food records that may be associated with changed eating habits during the data collection or underreporting of foods perceived as unhealthy. In YFS, information on childhood dietary habits was obtained with a nonquantitative food frequency questionnaire, but in adulthood a more detailed quantitative food frequency questionnaire providing an estimate of food consumption in grams per day was used [7]. Marked differences in the dietary assessment methods and definition of ideal diet in childhood at least partly explain the observed differences in having ideal diet. Physical activity and smoking were assessed by questionnaires in both cohorts, however, different questions and thus criteria for childhood ideal physical activity and childhood ideal smoking status were applied. Thirdly, because our study cohort was racially homogeneous, the generalizability of our results is limited to white Caucacian populations. During an extensive study period as in the STRIP and YFS, it is inevitable that loss to follow-up occurs. The characteristics of the remaining and discontinuing participants have been repeatedly compared, and few systematic differences have been found [15,16,28]. Here we observed some differences in CVH metrics between those participants who had requisite data to conduct this study and those who did not. In YFS, those included in this study had lower BMI, higher prevalence of ideal diet, and lower prevalence of ideal physical activity at baseline compared to nonparticipants. In STRIP, those included in this study had lower concentrations of total cholesterol and LDL cholesterol at the age of 15 years compared to nonparticipants. No other differences in baseline CVH metrics or serum lipids were found. We suspect that these differences do not substantially impact the results observed here. Major strengths of this study include the longitudinal study design and the long follow-up of participants who were well phenotyped in childhood and adulthood.

5. Conclusions

Higher number of ideal CVH metrics in childhood was associated with lower LV mass already at this early age. In addition, children with higher CVH score had better cardiac structure and function nearly three decades later as adults. Importantly, children who improved their CVH score from low to high between childhood and adulthood had similar measures of cardiac structure and function compared to those with persistently high CVH, suggesting that children with low CVH are not destined to maintain their higher risk provided their CVH can be improved. These data provide support for programs and interventions that target these health behaviors and factors in childhood as part of primordial and primary prevention of CVD.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ijcard.2016.12.117.

Sources of funding

STRIP was financially supported by Academy of Finland (grants 206374 and 251360); Juho Vainio Foundation; Finnish Ministry of Education and Culture; Finnish Cultural Foundation; the Finnish Foundation of Cardiovascular Research; Sigrid Juselius Foundation; Yrjö Jahnsson Foundation; Special Governmental Grants for Health Sciences Research, Turku University Hospital; and Turku University Foundation. YFS was financially supported by the Academy of Finland (grants 121584, 126925, 124282, 129378), the Social Insurance Institution of Finland, the Turku University Foundation, Special Federal Grants for University Hospitals, Juho Vainio Foundation, Paavo Nurmi Foundation, the Finnish Foundation of Cardiovascular Research, Orion-Farmos Research Foundation and the Finnish Cultural Foundation. CGM is supported by a National Heart Foundation of Australia Future Leader Fellowship (100849).

Conflicts of interest

This study has no conflicts of interest.

Acknowledgements

Biostatisticians Irina Lisinen, Johanna Ikonen and Noora Kartiosuo are acknowledged for statistical advise.

References

[1] J. Stamler, R. Stamler, J.D. Neaton, D. Wentworth, M.L. Daviglus, D. Garside, A.R. Dyer, K. Liu, P. Greenland, Low risk-factor profile and long-term cardiovascular and noncardiovascular mortality and life expectancy: findings for 5 large cohorts of young adult and middle-aged men and women, JAMA 282 (1999) 2012–2018.
[2] D.M. Lloyd-Jones, E.P. Leip, M.G. Larson, R.B. D'Agostino, A. Beiser, P.W. Wilson, P.A. Wolf, D. Levy, Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age, Circulation 113 (2006) 791–798.
[3] D.M. Lloyd-Jones, Y. Hong, D. Labarthe, D. Mozaffarian, L.J. Appel, L. Van Horn, K. Greenlund, S. Daniels, G. Nichol, G.F. Tomaselli, D.K. Arnett, G.C. Fonarow, P.M. Ho, M.S. Lauer, F.A. Masoudi, R.M. Robertson, V. Roger, L.H. Schwamm, P. Sorlie, C.W. Yancy, W.D. Rosamond, American Heart Association Strategic Planning Task Force and Statistics Committee, Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic impact goal through 2020 and beyond, Circulation 121 (2010) 586–613.
[4] C. Dong, T. Rundek, C.B. Wright, Z. Anwar, M.S. Elkind, R.L. Sacco, Ideal cardiovascular health predicts lower risks of myocardial infarction, stroke, and vascular death across whites, blacks, and hispanics: the northern Manhattan study, Circulation 125 (2012) 2975–2984.
[5] V. Xanthakis, D.M. Enserro, J.M. Murabito, J.F. Polak, K.C. Wollert, J.L. Januzzi, T.J. Wang, G. Tofler, R.S. Vasan, Ideal cardiovascular health: associations with biomarkers and subclinical disease and impact on incidence of cardiovascular disease in the Framingham offspring study, Circulation 130 (2014) 1676–1683.
[6] A.M. Shah, B. Claggett, A.R. Folsom, P.L. Lutsey, C.M. Ballantyne, G. Heiss, S.D. Solomon, Ideal cardiovascular health during adult life and cardiovascular structure and function among the elderly, Circulation 132 (2015) 1979–1989.
[7] T.T. Laitinen, K. Pahkala, C.G. Magnussen, J.S. Viikari, M. Oikonen, L. Taittonen, V. Mikkilä, E. Jokinen, N. Hutri-Kähönen, T. Laitinen, M. Kähönen, T. Lehtimäki, O.T. Raitakari, M. Juonala, Ideal cardiovascular health in childhood and cardiometabolic outcomes in adulthood: the Cardiovascular Risk in Young Finns Study, Circulation 125 (2012) 1971–1978.
[8] H. Aatola, N. Hutri-Kähönen, M. Juonala, T.T. Laitinen, K. Pahkala, V. Mikkila, R. Telama, T. Koivistoinen, T. Lehtimäki, J.S. Viikari, O.T. Raitakari, M. Kähönen, Prospective relationship of change in ideal cardiovascular health status and arterial stiffness: the Cardiovascular Risk in Young Finns Study, J. Am. Heart Assoc. 3 (2014), e000532.
[9] T.T. Laitinen, K. Pahkala, C.G. Magnussen, M. Oikonen, J.S. Viikari, M.A. Sabin, S.R. Daniels, O.J. Heinonen, L. Taittonen, O. Hartiala, V. Mikkilä, N. Hutri-Kähönen, T. Laitinen, M. Kähönen, O.T. Raitakari, M. Juonala, Lifetime measures of ideal cardiovascular health and their association with subclinical atherosclerosis: the Cardiovascular Risk in Young Finns Study, Int. J. Cardiol. 185 (2015) 186–191.
[10] K. Pahkala, H. Hietalampi, T.T. Laitinen, J.S. Viikari, T. Rönnemaa, H. Niinikoski, H. Lagström, S. Talvia, A. Jula, O.J. Heinonen, M. Juonala, O. Simell, O.T. Raitakari, Ideal cardiovascular health in adolescence: effect of lifestyle intervention and association with vascular intima-media thickness and elasticity (the Special Turku Coronary Risk Factor Intervention Project for Children [STRIP] study), Circulation 127 (2013) 2088–2096.
[11] C.S. Desai, H. Ning, K. Liu, J.P. Reis, S.S. Gidding, A. Armstrong, J.A. Lima, D.M. Lloyd-Jones, Cardiovascular health in young adulthood and association with left ventricular structure and function later in life: the Coronary Artery Risk Development in Young Adults Study, J. Am. Soc. Echocardiogr. 28 (2015) 1452–1461.
[12] D. Levy, R.J. Garrison, D.D. Savage, W.B. Kannel, W.P. Castelli, Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study, N. Engl. J. Med. 322 (1990) 1561–1566.
[13] G. de Simone, J.S. Gottdiener, M. Chinali, M.S. Maurer, Left ventricular mass predicts heart failure not related to previous myocardial infarction: the Cardiovascular Health Study, Eur. Heart J. 29 (2008) 741–747.
[14] G.C. Kane, B.L. Karon, D.W. Mahoney, M.M. Redfield, V.L. Roger, J.C. Burnett Jr., S.J. Jacobsen, R.J. Rodeheffer, Progression of left ventricular diastolic dysfunction and risk of heart failure, JAMA 306 (2011) 856–863.
[15] O. Simell, H. Niinikoski, T. Rönnemaa, O.T. Raitakari, H. Lagström, M. Laurinen, M. Aromaa, P. Hakala, A. Jula, E. Jokinen, I. Välimäki, J. Viikari, STRIP Study Group, 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 (2009) 650–655.
[16] M. Nupponen, K. Pahkala, M. Juonala, C.G. Magnussen, H. Niinikoski, T. Rönnemaa, J.S. Viikari, M. Saarinen, H. Lagström, A. Jula, O. Simell, O.T. Raitakari, Metabolic syndrome from adolescence to early adulthood: effect of infancy-onset dietary counseling of low saturated fat: the Special Turku Coronary Risk Factor Intervention Project (STRIP), Circulation 131 (2015) 605–613.
[17] O.T. Raitakari, M. Juonala, T. Rönnemaa, L. Keltikangas-Järvinen, L. Räsänen, M. Pietikäinen, N. Hutri-Kähönen, L. Taittonen, E. Jokinen, J. Marniemi, A. Jula, R. Telama, M. Kähönen, T. Lehtimäki, H.K. Åkerblom, J.S. Viikari, Cohort profile: the Cardiovascular Risk in Young Finns Study, Int. J. Epidemiol. 37 (2008) 1220–1226.
[18] M. Juonala, J.S. Viikari, M. Kähönen, L. Taittonen, T. Laitinen, N. Hutri-Kähönen, T. Lehtimäki, A. Jula, M. Pietikäinen, E. Jokinen, R. Telama, L. Räsänen, V. Mikkilä, H. Helenius, M. Kivimäki, O.T. Raitakari, Life-time risk factors and progression of carotid atherosclerosis in young adults: the Cardiovascular Risk in Young Finns Study, Eur. Heart J. 31 (2010) 1745–1751.
[19] R.M. Lang, M. Bierig, R.B. Devereux, F.A. Flachskampf, E. Foster, P.A. Pellikka, M.H. Picard, M.J. Roman, J. Seward, J.S. Shanewise, S.D. Solomon, K.T. Spencer, M.S. Sutton, W.J. Stewart, Chamber Quantification Writing Group, American Society of Echocardiography's Guidelines and Standards Committee, European Association of Echocardiography, Recommendations for chamber quantification: a report from the American Society of Echocardiography's guidelines and standards committee and the chamber quantification writing group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology, J. Am. Soc. Echocardiogr. 18 (2005) 1440–1463.
[20] S.F. Nagueh, O.A. Smiseth, C.P. Appleton, B.F. Byrd III, H. Dokainish, T. Edvardsen, F.A. Flachskampf, T.C. Gillebert, A.L. Klein, P. Lancellotti, P. Marino, J.K. Oh, B.A. Popescu, A.D. Waggoner, Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging, J. Am. Soc. Echocardiogr. 29 (2016) 277–314.
[21] H. Mikola, K. Pahkala, T. Rönnemaa, J.S. Viikari, H. Niinikoski, E. Jokinen, P. Salo, O. Simell, M. Juonala, O.T. Raitakari, Distensibility of the aorta and carotid artery and left ventricular mass from childhood to early adulthood, Hypertension 65 (2015) 146–152.
[22] S. Ruohonen, J.W. Koskenvuo, M. Wendelin-Saarenhovi, M. Savontaus, M. Kähönen, T. Laitinen, T. Lehtimäki, E. Jokinen, J. Viikari, M. Juonala, L. Taittonen, P. Tossavainen, M. Kallio, J.J. Bax, O. Raitakari, Reference values for echocardiography in middle-aged population: the Cardiovascular Risk in Young Finns Study, Echocardiography 33 (2016) 193–206.
[23] G. de Simone, S.R. Daniels, R.B. Devereux, R.A. Meyer, M.J. Roman, O. de Divitiis, M.H. Alderman, Left ventricular mass and body size in normotensive children and adults: assessment of allometric relations and impact of overweight, J. Am. Coll. Cardiol. 20 (1992) 1251–1260.
[24] M. Juonala, C.G. Magnussen, G.S. Berenson, A. Venn, T.L. Burns, M.A. Sabin, S.R. Srinivasan, S.R. Daniels, P.H. Davis, W. Chen, C. Sun, M. Cheung, J.S. Viikari, T. Dwyer, O.T. Raitakari, Childhood adiposity, adult adiposity, and cardiovascular risk factors, N. Engl. J. Med. 365 (2011) 1876–1885.
[25] C.G. Magnussen, J. Koskinen, M. Juonala, W. Chen, S.R. Srinivasan, M.A. Sabin, R. Thomson, M.D. Schmidt, Q.M. Nguyen, J.H. Xu, M.R. Skilton, M. Kähönen, T. Laitinen, L. Taittonen, T. Lehtimäki, T. Rönnemaa, J.S. Viikari, G.S. Berenson, O.T. Raitakari, A diagnosis of the metabolic syndrome in youth that resolves by adult life is associated with a normalization of high carotid intima-media thickness and type 2 diabetes mellitus risk: the Bogalusa Heart and Cardiovascular Risk in Young Finns Studies, J. Am. Coll. Cardiol. 60 (2012) 1631–1639.
[26] T. Katayama, N. Fujiwara, Y. Tsuruya, Factors contributing to left atrial enlargement in adults with normal left ventricular systolic function, J. Cardiol. 55 (2010) 196–204.
[27] M. Osranek, F. Bursi, K.R. Bailey, B.R. Grossardt, R.D. Brown Jr., S.L. Kopecky, T.S. Tsang, J.B. Seward, Left atrial volume predicts cardiovascular events in patients originally diagnosed with lone atrial fibrillation: three-decade follow-up, Eur. Heart J. 26 (2005) 2556–2561.
[28] M. Juonala, J. Juhola, C.G. Magnussen, P. Wurtz, J.S. Viikari, R. Thomson, I. Seppälä, J. Hernesniemi, M. Kähönen, T. Lehtimäki, M. Hurme, R. Telama, V. Mikkilä, C. Eklund, L. Räsänen, M. Hintsanen, L. Keltikangas-Järvinen, M. Kivimäki, O.T. Raitakari, Childhood environmental and genetic predictors of adulthood obesity: the Cardiovascular Risk in Young Finns Study, J. Clin. Endocrinol. Metab. 96 (2011) E1542–E1549.