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Cardiovascular health in adolescents with type 1 diabetes: The SEARCH CVD Study

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Abstract

Objective—In their Strategic Impact Goal Statement, the American Heart Association focused on primordial prevention of cardiovascular risk factors by defining metrics for ideal cardiovascular health (ICH). The prevalence of ICH among youth with type 1 diabetes is unknown. Youth with type 1 diabetes face an increased risk of cardiovascular disease (CVD) as they age. The purpose of this report was to examine the prevalence of ICH in a population of youth with type 1 diabetes and to examine the association of ICH with measures of cardiovascular structure and function.

Research Design and Methods—This report is based on SEARCH CVD an ancillary study to the SEARCH for Diabetes in Youth. A total of 190 adolescents with type 1 diabetes had complete data on all of the ICH metrics at baseline and had measures of arterial stiffness [pulse wave velocity (PWV), brachial distensibility (BrachD) and augmentation index (AIx)] and carotid

intima-media thickness completed at a follow-up visit (on average 5 years after baseline (interquartile range 4-5)).

Results—No subjects met the ICH criteria for all 7 metrics. Meeting an increasing number of ICH metrics was significantly associated with lower arterial stiffness [lower PWV of the trunk ($\beta=-0.02 \pm 0.01$; $p=0.004$) and AIx ($\beta=-2.2 \pm 0.66$; $p=0.001$), and increased BrachD ($\beta=0.14 \pm 0.07$; $p=0.04$)].

Conclusions—Increasing number of ICH metrics was significantly associated with decreased arterial stiffness, but prevalence of ICH in this population was low. Youth with type 1 diabetes could benefit from improvements in their cardiovascular health.

Keywords

Diabetes Mellitus; Type 1; Adolescent; Pulse Wave Analysis; Carotid Intima-Media Thickness

Introduction

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in the US (1). People with type 1 diabetes are at increased risk of CVD compared with the general population (2). The incidence of type 1 diabetes worldwide is increasing (3), and prevention of CVD in this high risk population is a clinical and public health priority (4).

With the growing recognition of a need to focus on the primordial prevention of CVD, the American Heart Association (AHA) published a definition for ideal cardiovascular health (ICH) metrics involving 7 modifiable health factors and behaviors (5). The ICH metrics included definitions of ideal, intermediate, and poor health for the following factors and behaviors: total cholesterol, blood pressure, fasting plasma glucose, smoking, body mass index (BMI), physical activity, and diet (5). Primordial prevention of risk factors to increase cardiovascular health is particularly relevant for childhood and adolescent populations (6).

In the United States, fewer than 1% of adults meet the criteria for ICH in all 7 metrics (7-10). Studies in Finland (11,12) and from NHANES data in the US (13), found that no adolescents or young adults met the ICH criteria for all 7 metrics. In the Special Turku Coronary Risk Factor Intervention Project for Children (STRIP) study, the number of ICH metrics was inversely associated with aortic intima-media thickness (aIMT) and directly associated with aortic elasticity (11). In the Cardiovascular Risk in Young Finns Study, the number of ICH metrics at the baseline visit was inversely associated with hypertension, metabolic syndrome, high low-density lipoprotein, and carotid artery intima-media thickness (cIMT) in adulthood (12).

There have not been any published studies on the prevalence of ICH in a population of youth or adults with type 1 diabetes. It is of particular interest to evaluate whether the ICH metrics are associated with improved measures of subclinical cardiovascular structure and function before overt clinical disease appears. A limited amount of data exists on the association between ICH metrics and cardiovascular disease outcomes in adults (8,10,14), and only two reports (11,12) included subclinical cardiovascular disease outcomes. Given the higher risk of CVD seen in those with type 1 diabetes, and the importance of establishing

healthy lifestyles in youth, the purpose of this report was to examine the prevalence of ICH in a population of adolescents and young adults with type 1 diabetes. Additionally, we sought to examine the association of ICH with sub-clinical measures of cardiovascular disease-arterial stiffness and cIMT.

Methods

Study Design and Subjects

Participants for this study were enrolled in SEARCH CVD, an ancillary study to the SEARCH for Diabetes in Youth Study conducted in 2 of the 6 SEARCH sites, Colorado and Ohio. SEARCH is a multicenter study conducting population-based ascertainment of non-gestational cases of physician-diagnosed diabetes in youth age < 20 years at diagnosis (15). SEARCH participants were eligible for SEARCH CVD if they had physician-diagnosed type 1 diabetes and had completed a baseline SEARCH visit when age 10 years or older, between 2004 and 2005 (16). The baseline SEARCH visit included questionnaires on demographics and medical history, self-reported dietary intake and physical activity patterns, and a brief clinical exam. A follow up SEARCH CVD visit was completed in 2009-2011 on eligible participants, to assess cardiovascular structure (cIMT) and function [arterial stiffness as measured by pulse-wave velocity (PWV), brachial distensibility (BrachD), and augmentation index (AIx)]. A total of 190 adolescents with type 1 diabetes participating in the longitudinal component of SEARCH CVD had complete data on all of the metrics to calculate ICH. Those without complete data that were excluded from these analyses were similar by gender, race, HbA_{1c}, BMI z-score, total cholesterol, AIx, BrachD, and cIMT of the carotid bulb. They were younger (14 years vs 15 year), had a shorter diabetes duration (3 years vs 5 years), lower PWV (5.5 m/sec vs. 5.9 m/sec), and had smaller mean cIMT of the common (0.44 mm vs. 0.47 mm) and internal (0.37 mm vs. 0.40 mm) carotids. The study was reviewed and approved by the appropriate local institutional review boards and all participants provided signed informed consent or assent.

Ideal Cardiovascular Health Metrics

ICH was defined in the AHA's Strategic Impact Goal Statement (5) as the simultaneous presence of never smoking, body mass index <85th percentile, 60 minutes of moderate- or vigorous-intensity activity every day, 4-5 components of a healthy diet (4.5 cups per day of fruits or vegetables, two 3.5 oz servings of fish per week, three 1-oz-equivalent servings of fiber-rich whole grains per day, <1500 mg of sodium per day, and 36 oz per week of sugar-sweetened beverages), total cholesterol <170 mg/dl, blood pressure <90th percentile, and fasting plasma glucose <100 mg/dl (5). There were only 2 individuals in this sample on hypertension medication and only one of these met the definition for ideal blood pressure, therefore medication use was not included in our definition of hypertension. Since the fasting plasma glucose metric was defined for the general population and not those with type 1 diabetes, we utilized the American Diabetes Association recommended goal of hemoglobin A1c (HbA_{1c}) <7.5% for adolescents and young adults (17) in place of the fasting plasma glucose metric. For the remaining metrics, we used the AHA definition where possible, as described in the following sections and in Table 2.

Health Factors

Blood pressure measurements (systolic and diastolic) were taken using an aneroid sphygmomanometer with the subject having been seated for at least 5 minutes. The average of three measurements was used. Study visits were conducted under conditions of metabolic stability with no episodes of diabetic ketoacidosis during the previous month, in the absence of recent acute infection, and after an 8 hour fast for measurement of lipids (total cholesterol and triglycerides), plasma glucose, and HbA_{1c}, as previously described (15,16). Participants were asked to avoid taking any medicines other than long-acting insulin the night before the blood draw. They were also asked to avoid strenuous exercise, smoking, or caffeinated drinks 12 hours before the clinic visit. Blood samples were processed at the local sites and shipped within 24 hours to the central laboratory for analysis (Northwest Lipid Metabolism and Diabetes Research Laboratories, University of Washington, Seattle, WA). HbA_{1c} was assayed using high-performance liquid chromatography (TOSOH Bioscience, San Francisco, CA). Measurements of total cholesterol and triglycerides were performed enzymatically using Roche reagent on the Roche Modular P autoanalyzer (Roche Diagnostics, Indianapolis, IN).

Health Behaviors

Smoking status was collected from a standardized questionnaire. Current smoking was defined as having smoked cigarettes on at least one of the preceding 30 days. Never smoking was defined as either never taking a single puff or never having smoked a whole cigarette. Height was measured with a stadiometer and weight was measured using a standardized weighing machine. A BMI z-score adjusted for age and sex was calculated using the Centers for Disease Control and Prevention national standards (18). The z-score was converted to a percentile in order to categorize participants for this analysis (ideal <85th percentile).

Physical activity was collected from questionnaire using questions developed from the Youth Risk Behavior Surveillance Survey (19). According to the AHA definition, ideal physical activity is defined as being moderately or vigorously active for at least 60 minutes per day for children <20 and for 150 minutes per week for adults ≥20 (5). The questions available did not make it possible to determine the exact number of minutes per week that participants were moderately or vigorously active. Specifically, subjects were asked: "On how many of the past 7 days did you exercise or participate in a physical activity for at least 20 minutes that made you sweat and breathe hard?". Therefore, we used a surrogate definition for ideal physical activity as follows: for adolescents <20 years, ≥20 minutes of activity that resulted in sweating or breathing hard daily; for adults ≥20 years and older, ≥20 minutes of activity that resulted in sweating or breathing hard 5 days a week or more.

Diet was collected using the SEARCH Food Frequency Questionnaire (FFQ), which has been previously described in detail (20,21). Participants completing the FFQ indicated if they had consumed the specified foods in the previous week. They also indicated the average portion and the number of days. The FFQ included approximately 85 food lines, which were subsequently condensed into food groups and common serving sizes (22). Nutrient and kilocalorie (kcal) consumption was estimated from the FFQ. We defined ideal

diet as at least 4 of the following: 4 servings of fruit or vegetables/day, 2 servings of fish/week, 3 servings of fiber-rich grains/day, <1500 mg sodium per day, 3 servings of sugar-sweetened beverages/week, scaled to a 2000 kcal/day diet.

Arterial Stiffness Measurements

The arterial stiffness measurements (PWV, AIx, and BrachD) were performed at the SEARCH CVD follow-up visit and have been previously described in detail (23). PWV was measured with a SphygmoCor SCOR-PVx System and recorded as the difference in the carotid-to-distal path length divided by the difference in R-wave-to-waveform foot times. The average of three different PWV values for the trunk (carotid-femoral) was used in the analysis. AIx was calculated as the difference between the primary (main outgoing wave) and the reflected wave of the central arterial waveform, expressed as a percentage of the central pulse pressure and adjusted to a standard heart rate of 75 beats per minute. We performed 3 measurements of resting AIx consecutively and only analyzed readings that fulfilled all of the manufacturer's quality control cut points. Reproducibility among the 3 readings was high with intraclass correlation coefficients between 0.7 and 0.9 for all AIx variables (23). BrachD was obtained using a DynaPulse Pathway instrument (Pulse Metric, Inc., San Diego, California) which performs waveform analysis of the arterial pressure signals obtained from a standard cuff sphygmomanometer from which to calculate distensibility, as previously described (24). For PWV and AIx, higher values indicate more arterial stiffness, and for BrachD, lower values indicate more stiffness.

Carotid IMT Measurement—Guidelines for cIMT measurement in a pediatric population were followed for this study (25). The cIMT measurement was obtained from both sides at the common, bifurcation (bulb) and internal carotid arteries using high-resolution B-mode ultrasonography with a GE Vivid 7 ultrasound imaging system (GE Medical Systems, Wauwatosa, WI). A minimum of a 10 cm length was used in the common carotid artery. Correct placement was confirmed using pulsed wave Doppler. The far wall mean and maximal IMT were read from the images using a manual trace method with Amicas-Vericis (Merge Inc., Chicago, IL) software. An experienced sonographer that was blinded to the health status of the child performed manual trace of 3 still images at the peak of the R wave for all segments and all angles. The average intrasubject coefficient of variation for the 3 measurements was no more than 5.4% for any of the sites. The mean cIMT from each of the predetermined angles (90, 120, and 150 degrees on the right; 210, 240, and 270 degrees on the left) was used for this analysis.

Statistical Analyses

Parametric continuous data are presented as means \pm the standard deviation. Triglyceride and plasma glucose values were not normally distributed; they were log-transformed and geometric means are shown. Categorical data are presented as number of subjects and percents. To test for differences between groups we used the t-test for parametric continuous data and the chi-square test for categorical data.

Multivariate linear regression models examined the relationships between the individual ICH metrics, as well as the number of metrics that met the ideal health criteria, and each of

the sub-clinical cardiovascular outcomes: PWV of the trunk, BrachD, AIx and cIMT, controlling for other risk factors and potential confounders. Variables were selected to be included in the model based on their significance in previous work. Baseline covariates included demographics (age, sex, race/ethnicity, site), duration of diabetes (months), and the time between the baseline and the follow up visits. All analyses were performed using SAS/STAT software, Version 9.3 of the SAS System for Windows (SAS Institute Inc., Cary, NC, USA).

Results

Characteristics of the study population are presented in Table 1. The median age of participants at the baseline visit was 15 (interquartile range 13-17) years, and the median duration of diabetes was 5 (interquartile range 2-8) years. At the 2nd visit, the median age was 20 (interquartile range 18-22) years and duration of diabetes was 10 (interquartile range 7-13) years. Slightly more than half of the population was male (57.4%) and the majority were white, non-Hispanic (89.0%).

The prevalence of the different ICH metrics is presented in Table 2. A large number of subjects met the goals for smoking and blood pressure (88.4% and 80.5%, respectively). More than two-thirds of the population met the goal for BMI (67.4%). The goal for total cholesterol was met by 63.7%. The proportion meeting the HbA_{1c} goal of <7.5% was only 29.0%. Only 12.6% met the modified criteria for physical activity, and no subjects met the goals for diet. Of the individual components of the healthy diet, 19.5% met the goal for fruit/vegetable consumption, 4.3% met the goal for fish consumption, and 63.7% met the goal for sugar-sweetened beverage consumption. No subjects met the goal for fiber-rich whole grains or sodium consumption.

Figure 1 presents the overall number of ICH metrics that were met. No subjects met the goals for all 7 metrics and only 2.1% met the definition for 6 metrics. The majority of the youth in this population met 3 or 4 metrics (34.7% and 30.5%, respectively). 1.1% did not meet any single goal.

Table 3 presents the results of multiple linear regression models adjusted for age, sex, site, race, diabetes duration, and time between the two visits. There were no significant associations between any single ICH metric and IMT of the internal carotid or bulb. Meeting the BMI goal was independently associated with reduced PWV of the trunk ($\beta = -0.06 \pm 0.02$; $p = 0.005$) and increased BrachD ($\beta = 0.43 \pm 0.16$; $p = 0.009$). The metrics for total cholesterol ($\beta = -3.7 \pm 1.6$; $p = 0.03$), blood pressure ($\beta = -4.7 \pm 2.0$; $p = 0.02$), and HbA_{1c} ($\beta = -6.3 \pm 1.7$; $p < 0.001$) were significantly associated with reduced AIx in the unadjusted models, but were attenuated in the adjusted model ($p = 0.06$, $p = 0.07$, and $p = 0.11$; respectively). Meeting the physical activity goal was significantly associated with reduced cIMT of the common carotid ($\beta = -0.05 \pm 0.02$; $p = 0.002$). Meeting an increasing number of ICH metrics (model 2) was significantly associated with decreased PWV of the trunk ($\beta = -0.02 \pm 0.01$; $p = 0.004$) and AIx ($\beta = -2.2 \pm 0.66$; $p = 0.001$), and increased BrachD ($\beta = 0.14 \pm 0.07$; $p = 0.04$), but not with decreased cIMT of the common carotid ($\beta = -0.003 \pm 0.005$; $p = 0.46$).

Discussion

This is the first report on the prevalence of ICH, as defined by the AHA, in a population of youth with type 1 diabetes and on the association with subsequent subclinical measures of cardiovascular disease. We found that no youth in this population simultaneously met all 7 metrics for ICH, and in particular, the prevalence of ideal physical activity and diet were low. The majority of subjects met the ideal criteria for 3 or 4 metrics. Moreover, meeting an increasing number of ICH metrics was significantly associated with lower arterial stiffness. Our results in youth with type 1 diabetes confirm and extend findings of other studies in youth and adults without diabetes that the prevalence of ICH is low (7-9,12,26,27) and ICH is associated with adverse cardiovascular outcomes (11,12).

Diet has previously been examined in other SEARCH reports. Mayer-Davis, et al. (21) comprehensively examined diet in youth with type 1 and type 2 diabetes (nutrients, total and saturated fat, sugar-sweetened beverages, fruits, vegetables, and whole grains consumption) compared with diet recommendations from the American Diabetes Association, AHA, Healthy People 2010. Similar to this report, diet fell short of national recommendations for healthy diet, and no subjects met the recommendations for whole grain consumption. In other categories not assessed by the AHA diet definition, only 6.5% met the recommendations for saturated fat, 10.6% for total fat, 6.4% for fiber, and 15.6% for vitamin E. Physical activity was examined in a previous report from the SEARCH Case-Control Study, another ancillary study to SEARCH (28). In this study, physical activity was assessed with the 3-Day Physical Activity Recall questionnaire, with information on moderate and vigorous intensity activities collected in 30-minute time blocks, averaged over the 3 days. Among male subjects with type 1 diabetes, 82.3% met the recommendation for at least 2 time-blocks of moderate or vigorous intensity activity per day, and among female subjects, 81.3% met the recommendation. Since activity was averaged over 3 days, it is not possible to say how many of these subjects would meet the recommended activity level for each of the 3 days, and also not possible to say how many of these would achieve that level of activity for 7 days, as per the AHA-definition for ideal physical activity. This also suggests that reports on recommended levels of physical activity are very sensitive to the measures and definitions used.

In the US, estimates for ICH from NHANES for adolescents aged 12-19 years were similar to our estimates, with no subjects meeting the ideal criteria for all 7 metrics (13). Ideal smoking was less prevalent in the general US population (66% in males and 70% in females) compared to the 88.4% in our study. While the prevalence of ideal total cholesterol was slightly lower in our study (63.7% vs 72% in males and 65% in females), ideal BMI was very similar (67.4% vs. 66% in males and 67% in females). The prevalence of ideal blood pressure was also similar between the studies (80.5% in our study vs. 77.7% in males and 90% in females). Physical activity was higher in the general US population (67% in males and 43.5% in females vs. 12.6% in our study). This is likely due to differences in how physical activity was reported. Due to improvements in the physical activity measure in NHANES, only data for 2007-2010 were reported for this metric. Similar to our study, no subjects in the general US population met the ideal criteria for diet.

Two other studies looked at the AHA defined ICH in an adolescent population, however, without diabetes. In the Cardiovascular Risk in Young Finn's Study (12), no subjects met all 7 metrics for ideal cardiovascular health, and similar to our study, 36.4% met 3 metrics and 34.3% met 4 metrics. Meeting blood pressure goals was similar (82.2% in Finland compared with 80.5% in the current study). More subjects met the BMI (85.6% vs. 67.4%) and diet goals (24.3% vs. 0.0%) in the Cardiovascular Risk in Young Finn's Study compared with the current study. Diet was assessed in the Cardiovascular Risk in Young Finn's Study in children by a nonquantitative food frequency questionnaire that did not permit assessment of sodium or whole grain consumption; therefore, differences between the two studies may reflect differences in how the diet goal was defined. In contrast, fewer subjects met the physical activity (6.9% vs. 12.6%), smoking (22.4% vs. 88.4%), and total cholesterol goals (33.2% vs. 63.7%) in the Cardiovascular Risk in Young Finn's Study compared with SEARCH CVD. The Cardiovascular Risk in Young Finn's Study was able to assess physical activity according to the AHA definition of 60 minutes or more of moderate or vigorous physical activity per day. We were unable to fully implement this definition.

In the STRIP study, a study designed to look at the effect of dietary counseling on risk factors for atherosclerosis (11), no subjects met all 7 metrics for ideal cardiovascular health at any age. While the intervention did result in decreased intakes of saturated fat, the ideal diet was the least often met of all ICH metrics. In contrast to our study, in which no subjects met the ideal goal for whole-grains, nearly half of the STRIP study participants met the goal for whole grain intake. This may be due to the modified definition that was used for the whole grain metric in which only 2 or more servings per day was considered ideal, compared to the AHA definition of 3 or more servings per day. Very few met the ideal goal for sodium consumption, similar to our findings, where none of the participants met the ideal sodium consumption metric. Physical activity, which was calculated using metabolic equivalents (MET) of leisure-time sports and activities, was higher in the STRIP study (>40% at all ages) compared to either the Cardiovascular Risk in Young Finn's Study (6.9%) or the current study (12.6%).

A low prevalence of ICH has also been reported in other studies of non-diabetic adults. Multiple studies have reported that fewer than 1% of adults meet the goals for all 7 metrics (7-9,26,27). Prevalence of ICH for 5 or more metrics ranged from 5.3% (9) to 18.3% (26). Data from the National Health and Nutrition Examination Survey showed that the prevalence of ICH declines with age (7). Similar to our findings in youth, in several studies diet was the area with the lowest adherence to the proposed goal, between 0.4% and 38.7% (7-10,26), although the 38.7% was obtained from a study that only had access to diet information on fruit and vegetable consumption (9). Meeting the physical activity goals varied substantially among studies, but was generally higher than in the current study (range: 23.8%-60.3% vs. 12.6%) (7-10,26).

We found that meeting the ideal BMI metric was independently associated with reduced arterial stiffness and that meeting the ideal physical activity metric was independently associated with reduced cIMT of the common carotid. We also found that the overall number of metrics meeting the goals for ICH was significantly associated with decreased arterial stiffness (PWV, BrachD, and AIX), but not with cIMT. This may be due to the

relatively young age of our population, when age-related cIMT changes may be minimal. Supporting this notion, in the Cardiovascular Risk in Young Finns Study, the number of ICH metrics present in childhood (mean age 15 years) was significantly associated with high-risk cIMT in adulthood after a mean follow-up time of 21 years (OR 0.75; 95% CI 0.60-0.94) (12). However, in the STRIP study, an inverse association between the number of ICH metrics and aIMT was found in the adolescent population (11). We found that ICH was consistently associated with a variety of measures of decreased arterial stiffness indicating a detectable effect on vascular function even at this relatively early age. Cardiovascular disease incidence rates have been reported to be inversely associated with the number of ICH goals met in several studies in adults (8,10,27). ICH has also been linked to decreased mortality due to cardiovascular disease in adults (14,26).

Our study has some limitations. Physical activity and diet were self-reported and could have been affected by poor recall. Since the validity of food frequency questionnaires has been questioned in younger populations, only youth over the age of 10 provided diet information (21). The physical activity questionnaire did not collect minutes of moderate and vigorous intensity activity, so we are unable to determine how well this population would adhere to the AHA recommended physical activity levels. We modified the ideal cardiovascular health definitions by substituting HbA_{1c} for the plasma glucose metric because our population of youth with type 1 diabetes will not be able to meet the definition for ideal plasma glucose. While we used a cutpoint of 7.5% based on the American Diabetes Association recommended goal of HbA_{1c} <7.5% for adolescents and young adults (17), this is still an arbitrary cutpoint and arguments for other cutpoints could be made. The use of more stringent cutpoints would shift the distribution of the number of ICH health metrics towards fewer metrics meeting the ideal criteria. However, in multivariate linear regression models for the number of ICH metrics on the various outcomes, use of different cutpoints (7% and 6.5%) did not significantly alter the results. In addition, 29% of our population met this goal, which is similar to the 21% of 13 to younger than 20 year olds that met this goal in the T1D Exchange registry (29), demonstrating that our population is comparable in this metric to other populations of adolescents with T1D. This study included youth with type 1 diabetes that were enrolled in the SEARCH CVD study and with complete information on ICH and therefore, the potential exists that this study population would not be representative of the larger SEARCH population or those with type 1 diabetes outside of the SEARCH study. SEARCH CVD eligibility was partially based on age, making the mean age of SEARCH CVD participants older than other published reports from SEARCH. In addition, the SEARCH CVD population includes a higher proportion of non-Hispanic white participants than other published SEARCH reports (30,31). However, the distribution of age at diagnosis, and estimates for some of the basic characteristics related to ICH from the current study population were similar to published estimates of those with type 1 diabetes from the larger SEARCH cohort (30,31). Automatic edge detection for cIMT measurement was not available at the time that this study was initiated. However, all measurements were performed by an experienced sonographer at each site.

In conclusion, youth with type 1 diabetes face an increased risk for cardiovascular disease morbidity and mortality (22) and thus, achieving cardiovascular health needs to be a priority. The significant association between ICH metrics and subsequent measures of subclinical

cardiovascular disease (arterial stiffness) in an adolescent and young adult population with type 1 diabetes highlights the critical importance of addressing cardiovascular health at a young age. Our data suggest that youth with type 1 diabetes could benefit from improvements in their cardiovascular health.

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Abbreviations

| | |
|---------------|--|
| CVD | cardiovascular disease |
| AHA | American Heart Association |
| ICH | ideal cardiovascular health |
| BMI | body mass index |
| STRIP | Special Turku Coronary Risk Factor Intervention Project for Children |
| aIMT | aortic intima-media thickness |
| cIMT | carotid artery intima-media thickness |
| SEARCH | SEARCH for Diabetes in Youth Study |
| PWV | pulse-wave velocity |
| BrachD | brachial distensibility |
| AIx | augmentation index |
| HbA1c | hemoglobin A1c |
| FFQ | food frequency questionnaire |
| kcal | kilocalorie |

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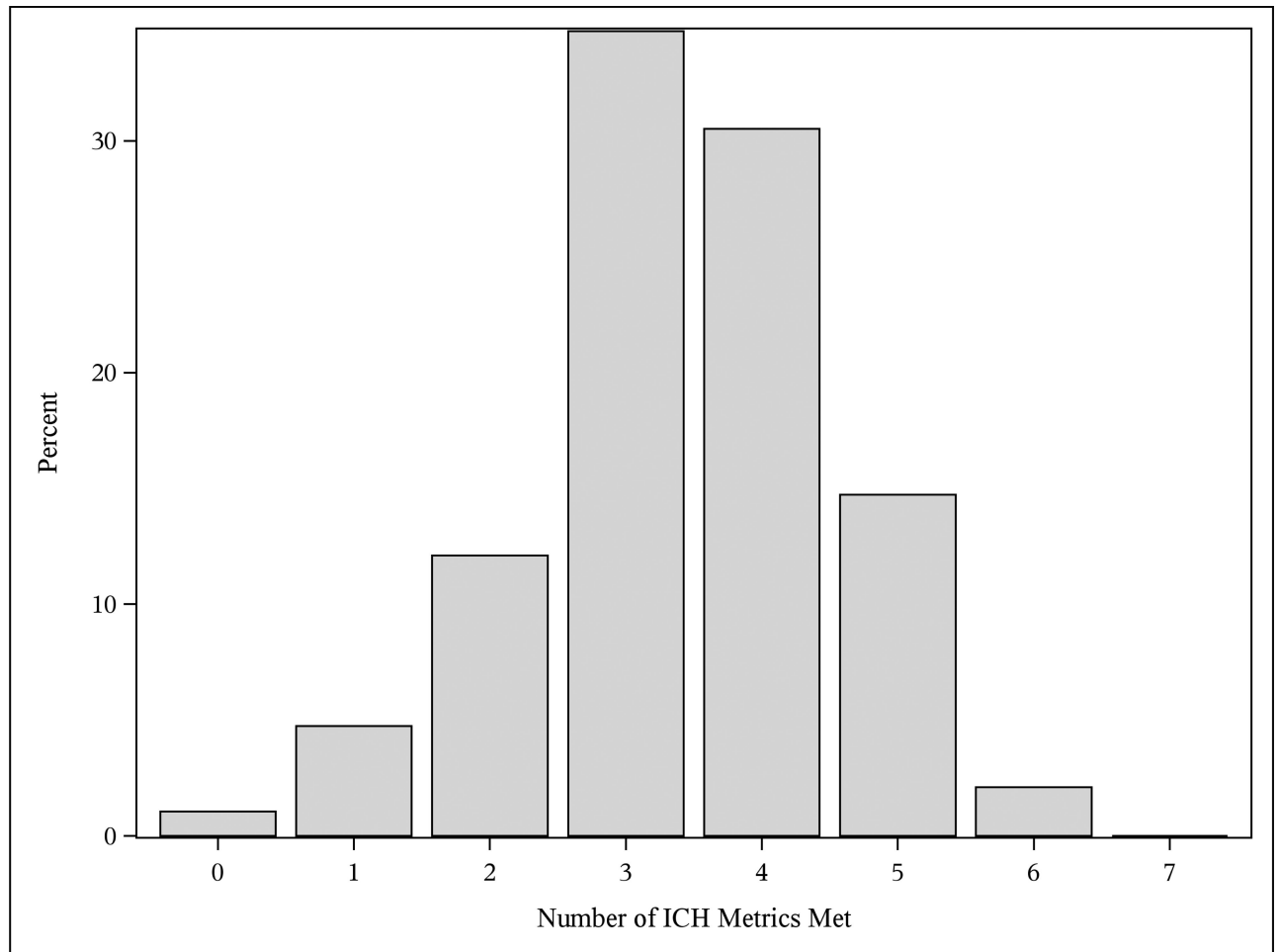


Figure 1.
Number of individual ICH metrics met by study participants.

Table 1

Characteristics of the study population (N=190)

| Characteristic | |
|--|--------------------|
| Age at baseline (years), median (25 th -75 th percentiles) | 15 (13-17) |
| Diabetes duration at baseline (years), median (25 th -75 th percentiles) | 5 (2-8) |
| Males, N (%) | 109 (57.4) |
| Race/ethnicity, N (%) | |
| White | 169 (89.0) |
| Black | 13 (6.8) |
| Hispanic | 6 (3.2) |
| Other | 2 (1.1) |
| Site, OH N (%) | 126 (66.3) |
| HbA _{1c} at baseline (%), mean (\pm SD) | 8.2 (\pm 1.4) |
| Waist circumference at baseline (cm), mean (\pm SD) | 76.0 (\pm 11.3) |
| Total cholesterol at baseline (mg/dl), median (25 th -75 th percentiles) | 161 (145-180) |
| Age at CVD visit (years), median (25 th -75 th percentiles) | 20 (18-22) |
| Duration between visits (years), median (25 th -75 th percentiles) | 5 (4-5) |
| PWV trunk (m/sec) [*] , median (25 th -75 th percentiles) | 5.9 (5.4-6.7) |
| BrachD (% change/mmHg) [*] , median (25 th -75 th percentiles) | 6.0 (5.2-6.8) |
| AIx (%),mean (\pm SD) [*] | 0.12 (\pm 10.7) |
| Carotid bulb IMT (mm), mean (\pm SD) [*] | 0.47 (\pm 0.07) |
| Common carotid IMT (mm), mean (\pm SD) [*] | 0.47 (\pm 0.07) |
| Internal carotid IMT (mm) [*] , median (25 th -75 th percentiles) | 0.40 (0.36-0.46) |

PWV: pulse wave velocity; AIx: augmentation index; BrachD: brachial distensibility; IMT: intima-media thickness

^{*} Measures taken at SEARCH CVD follow-up visit

Table 2

Prevalence of Ideal Cardiovascular Health Metrics

| Metric | Goal | Prevalence of ICH | |
|---------------------------|---|-------------------|--|
| | | N (%) | |
| Smoking | Never smoked | 168 (88.4) | |
| BMI | For adolescents aged <20 years: <85 th percentile. For adults 20 and over: <25 kg/m ² | 128 (67.4) | |
| Physical activity | For adolescents aged <20 years: 20 minutes of physical activity (sweating or breathing hard) 7 days per week; for adults 20 and over: 20 minutes of physical activity 5 or more days per week | 24 (12.6) | |
| Healthy diet score * | 4-5 healthy diet components (listed below) | 0 (0.0) | |
| Fruit/vegetables | 4 servings/day | 37 (19.5) | |
| Fish | 2 servings/week | 8 (4.2) | |
| Fiber-rich whole grains | 3 servings/day | 0 (0.0) | |
| Sodium | <1500 mg/day | 0 (0.0) | |
| Sugar-sweetened beverages | 3 servings/week | 121 (63.7) | |
| Total cholesterol | For adolescents aged <20 years: <170 mg/dl. For adults 20 and over: <200 mg/dl | 121 (63.7) | |
| Blood pressure | For adolescents aged <20 years: <90 th percentile. For adults 20 and over: <120/<80 | 153 (80.5) | |
| HbA _{1c} | <7.5% | 55 (29.0) | |

* Scaled to 2,000 kcal/day

Table 3
Multiple Linear Regression of Ideal Cardiovascular Health on Measures of Arterial Stiffness and Mean Carotid IMT

| Variable | PWV trunk | | BrachD | | AIx | |
|---|---------------------|--------------------|-------------------|-------------------|--------------------|-------------------|
| | Unadjusted | Adjusted* | Unadjusted | Adjusted* | Unadjusted | Adjusted* |
| Model 1: Individual ideal health metrics [†] | | | | | | |
| Smoking | -0.04 ±0.03, 0.15 | 0.02 ±0.03, 0.46 | -0.28 ±0.23, 0.23 | -0.29 ±0.25, 0.24 | -3.2 ±2.4, 0.18 | -3.5 ±2.4, 0.15 |
| BMI | -0.07 ±0.02, <0.001 | -0.06 ±0.02, 0.005 | 0.46 ±0.16, 0.004 | 0.43 ±0.16, 0.009 | 0.44 ±1.7, 0.80 | 0.90 ±1.6, 0.58 |
| Physical activity | 0.04 ±0.03, 0.17 | 0.02 ±0.03, 0.41 | 0.14 ±0.23, 0.54 | 0.13 ±0.22, 0.57 | 0.12 ±2.7, 0.97 | -1.4 ±2.4, 0.56 |
| Total cholesterol | -0.01 ±0.02, 0.48 | -0.01 ±0.02, 0.52 | -0.16 ±0.16, 0.32 | -0.12 ±0.16, 0.45 | -3.7 ±1.6, 0.03 | -2.9 ±1.5, 0.06 |
| Blood pressure | -0.07 ±0.02, 0.004 | -0.04 ±0.02, 0.09 | 0.41 ±0.19, 0.03 | 0.29 ±0.19, 0.13 | -4.7 ±2.0, 0.02 | -3.5 ±1.9, 0.07 |
| HbA _{1c} | -0.03 ±0.02, 0.14 | -0.03 ±0.02, 0.21 | 0.03 ±0.17, 0.84 | 0.17 ±0.18, 0.35 | -6.3 ±1.7, <0.001 | -2.8 ±1.7, 0.11 |
| Model 2: | | | | | | |
| Number of ideal health metrics | -0.03 ±0.01, 0.001 | -0.02 ±0.01, 0.004 | 0.09 ±0.07, 0.16 | 0.14 ±0.07, 0.04 | -2.5 ±0.69, <0.001 | -2.2 ±0.66, 0.001 |

| | cIMT CC | | cIMT IC | | cIMT Bulb | |
|---|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|
| | Unadjusted | Adjusted* | Unadjusted | Adjusted* | Unadjusted | Adjusted* |
| Model 1: Individual ideal health metrics [†] | | | | | | |
| Smoking | 0.0008 ±0.02, 0.96 | 0.03 ±0.02, 0.10 | -0.01 ±0.02, 0.52 | 0.005 ±0.02, 0.81 | -0.003 ±0.02, 0.86 | 0.002 ±0.02, 0.88 |
| BMI | -0.01 ±0.01, 0.38 | -0.001 ±0.01, 0.90 | -0.02 ±0.01, 0.12 | -0.02 ±0.01, 0.19 | -0.02 ±0.01, 0.14 | -0.01 ±0.01, 0.23 |
| Physical activity | -0.04 ±0.02, 0.03 | -0.05 ±0.02, 0.002 | 0.002 ±0.02, 0.92 | -0.004 ±0.02, 0.82 | 0.02 ±0.02, 0.26 | 0.01 ±0.02, 0.48 |
| Total cholesterol | 0.01 ±0.01, 0.47 | 0.001 ±0.01, 0.92 | 0.007 ±0.01, 0.61 | 0.0001 ±0.01, 0.99 | -0.005 ±0.01, 0.67 | -0.005 ±0.01, 0.64 |
| Blood pressure | -0.02 ±0.01, 0.06 | -0.02 ±0.01, 0.07 | -0.03 ±0.02, 0.07 | -0.02 ±0.02, 0.12 | -0.03 ±0.01, 0.02 | -0.02 ±0.01, 0.11 |
| HbA _{1c} | 0.02 ±0.01, 0.10 | 0.01 ±0.01, 0.32 | 0.02 ±0.01, 0.16 | 0.02 ±0.01, 0.27 | -0.005 ±0.01, 0.67 | 0.002 ±0.01, 0.88 |
| Model 2: | | | | | | |
| Number of ideal health metrics | -0.003 ±0.005, 0.50 | -0.003 ±0.005, 0.46 | -0.003 ±0.005, 0.53 | -0.005 ±0.005, 0.36 | -0.007 ±0.005, 0.14 | -0.007 ±0.005, 0.16 |

cIMT: Carotid IMT; CC: Common Carotid; IC: Internal Carotid

* Adjusted for the other individual ideal health metrics (model 1) in the model and age, sex, site, race, diabetes duration, and distance between 1st and 2nd visit

[†]For Model 1, factors were included in a single model to test the independent effect of each; diet could not be included because no subjects met the criteria for ideal diet