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Risk Factors of Premature Atherosclerotic Cardiovascular Disease in China: A Longitudinal Analysis of the China Health and Nutrition Survey Cohort

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Abstract

The burden of premature atherosclerotic cardiovascular disease (ASCVD) has increased rapidly in China. Using the China Health and Nutrition Survey (CHNS) data, we assessed the risk factors of premature ASCVD (age of diagnosis: <55 years for men and <65 years for women). Propensity score matching was used to reduce selection bias. Multivariable Cox proportional-hazards analyses indicated that factors associated with increased risk of premature ASCVD included hypertension (adjusted hazard ratio [$HR_{adj.}$] = 1.68), obesity ($HR_{adj.}$ = 1.64), and high carbohydrate intake ($HR_{adj.}$ = 1.46). Conversely, participants with medical insurance ($HR_{adj.}$ = 0.42), high urbanization index ($HR_{adj.}$ = 0.53), and high household income ($HR_{adj.}$ = 0.48) had lower risk of premature ASCVD. When comparing premature vs non-premature ASCVD participants, those who were obese ($HR_{adj.}$ = 2.08) or living in more urbanized areas had higher hazards of early onset ($HR_{adj.}$ = 2.29).

Keywords

China Health and Nutrition Survey, cohort study, early onset, premature atherosclerotic cardiovascular disease, risk factors

What We Already Know

- In China, the burden of atherosclerotic cardiovascular disease (ASCVD) is rapidly and significantly increasing.
- Studies in China and abroad have shown the onset of ASCVD tends to start at a younger age.

What This Article Adds

- This article revealed factors associated with premature and non-premature ASCVD among the Chinese population. Risk factors of premature ASCVD differed from those of non-premature ASCVD.
- Factors associated with premature ASCVD included blood pressure, body mass index, carbohydrate intake, medical insurance, urbanization index, and household income.
- Body mass index and urbanization index were associated with an increased risk of early onset of ASCVD.

Introduction

Cardiovascular disease (CVD) is the leading cause of death in China. In 2019, CVD deaths accounted for 46.74% and 44.26% of the total deaths in rural and urban areas, respectively.[1] Between 1990 and 2016, the age-standardized incidence rate (ASIR) of CVD increased by 14.7%.[2] An important feature of CVD epidemiology in China is the rapid and significant increase in the burden of atherosclerotic cardiovascular disease

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(ASCVD), including coronary heart disease, stroke, and peripheral vascular disease.[3] Approximately 2.4 million people died of ASCVD in 2016, accounting for 61% of CVD deaths and 25% of all deaths, increasing from about 1 million ASCVD deaths in 1990 (accounting for 40% of CVD deaths and 11% of all deaths).[3]

Studies in China and abroad have shown the onset of ASCVD tends to start at a younger age.[4-6] As reported in a study[7] from the United States, the overall proportion of acute myocardial infarction (AMI) hospital admissions increased steadily, from 27% in 1995 to 32% in 2014, and the increased proportion was mainly attributed to young patients. Another US study[8] based on the National Inpatient Sample (NIS) data has found acute ischemic stroke (AIS) hospitalization rates increased among the three younger groups for all race/ethnic groups from 2003 to 2012 (18-34 years: by 27.3%; 35-44 years: by 35.6%; and 45-54 years: by 20.5%). Similar findings have been reported from Denmark.[9] The American College of Cardiology (ACC) defines ASCVD occurring in males aged <55 years or females aged <65 years as premature ASCVD.[10]

Prior research has established risk factors for ASCVD onset,[5,11-13] but few prediction models have been tailored to and specifically validated in the younger population which is exposed to premature ASCVD risk, especially concerning some behavioral risk factors, such as diet, exercise, and weight status, that are essential for ASCVD primary prevention. Although there is a widely used 10-year ASCVD risk assessment tool—China-PAR, specifically tailored for the Chinese population,[14] it does not reveal possible risk factors for early onset. In addition, premature ASCVD is associated with other health and excessive socioeconomic burdens, such as increased cancer risk,[15] potential lifetime productivity loss, and increased lifetime health care use.[16]

The purpose of this longitudinal study is to explore risk factors for the onset of premature ASCVD in the Chinese population and provide recommendations for individual-tailored prevention strategies to effectively reduce the risk of premature ASCVD development among the Chinese population.

Methods

Study Participants and Data Source

This observational study was based on the data from the China Health and Nutrition Survey (CHNS) program, an ongoing multipurpose longitudinal household survey initiated in 1989, with a total of 10 rounds already completed. The CHNS used a multistage random-cluster process to draw the sample from the original eight provinces to final 15 provinces: Heilongjiang, Liaoning, Beijing, Henan, Jiangsu, Zhejiang, Shanghai, Shandong, Hubei, Hunan, Shaanxi, Yunnan, Chongqing, Guizhou, and Guangxi, which varied in demography, geography, economic development, and public resources. A detailed description of CHNS has been published previously.[17] CHNS data are publicly accessible, and the study protocols were approved by the institutional review boards of the University of North Carolina (USA) and the National Institute of Nutrition and Food Safety (China).[17] Each participant voluntarily signed a written informed consent before recruitment in CHNS.

For this study, we used seven waves of the survey conducted in 1997, 2000, 2004, 2006, 2009, 2011, and 2015, with the earliest wave with detailed survey information treated as the baseline (https://www.cpc.unc.edu/projects/china/data/datasets, accessed on March 13, 2022). Adults aged 18 years and above were included in the present analysis, for whom questionnaires and anthropometric data were collected during at least two waves. We excluded participants with ASCVD at baseline. Our final analytic sample consisted 16 965 participants and 66 658 observations (median time of follow-up: 9 years) (Supplementary Figure 1).

Outcome Measurement

The primary endpoint was the ASCVD event. The participants were asked to report their ASCVD event history with a questionnaire-based interview at the baseline and each follow-up. The questions were posed as follows: (1) "Has a doctor ever given you the diagnosis of myocardial infarction? If yes, how old were you when the doctor told you this (years), and how old were you when you had this problem the most recent time (years)?" (2) "Has a doctor ever given you the diagnosis of stroke or transient ischemic attack? If yes, how old were you when you were first diagnosed with stroke or transient ischemic attack (years), and how old were you when you had this problem the most recent time (years)?" For each survey, diagnosis of ASCVD was confirmed if at least one of the two answers was "yes" and the age of onset was reported. Premature ASCVD was defined as occurring in men aged under 55 years and in women aged under 65 years.[18] ASCVD events that happened beyond the early onset age were defined as non-premature ASCVD events (men aged $\geq$ 55 years and women aged $\geq$ 65 years) (Supplementary Figure 1).

Independent Variable

Twenty factors potentially associated with the development of ASCVD were examined in this study, including age, sex, education, medical insurance, marital status, smoking status, alcohol, tea, or coffee drinking behaviors, physical activity, hypertension and diabetes disease history, body mass index (BMI), urbanization index, household income, energy, carbohydrate, fat, or protein intake, and waist circumference (WC). The selection of targeted independent variables was based on clinical importance, scientific knowledge, and risk factors identified in published studies.[3,5,19] Supplementary Table 1 shows how the variables were assessed in the survey and their operational definitions for this study.

Statistical Analysis

Due to the low prevalence of premature and non-premature ASCVD events in this cohort (premature ASCVD 1.37%, non-premature ASCVD 0.68%), to avoid potential estimation bias associated with imbalanced data, propensity score matching (PSM)[20] was used to construct the dataset for analysis, while controlling for age and sex differences. To ensure sufficient variability in comparison subjects, we matched each premature and non-premature ASCVD case with three non-ASCVD comparisons, respectively, based on age, sex, and follow-up time, using nearest-neighbor matching with a caliper distance of 0.2 without replacement.[20] The PSM analysis was performed in R ("MatchIt" package).

Frequencies and proportions were reported for categorical variables; means and standard deviations were reported for continuous variables unless indicated otherwise. A correlation matrix was used to evaluate all explanatory variables for collinearity. Participants' sociodemographic characteristics, health behaviors, and disease history were compared between matched premature and non-premature ASCVD cases and their non-ASCVD comparisons using chi-square, two-sample, and Kruskal-Wallis H tests where appropriate.

To identify factors associated with premature ASCVD and non-premature ASCVD, three types of comparisons were made: (1) premature ASCVD vs non-ASCVD, (2) non-premature ASCVD vs non-ASCVD, and (3) premature ASCVD vs non-premature ASCVD. For each of the comparisons, univariate Cox proportional regression analysis was performed to examine unadjusted associations between each factor and the corresponding outcome. All regression analyses were stratified by the case and comparison matching group to consider the matching effect. Factors that showed a trend toward significance with a $P < .1$ in the unadjusted analysis were included in the multivariable regression models to assess the adjusted association. Statistical analyses were performed using rms in R (version 4.1.3; http://www.r-project.org). All tests were two-sided, and $P < .1$ and $P < .05$ were considered to be statistically significant in unadjusted analyses and multivariable analyses, respectively.

Results

Participants

Of participants included in analysis, 8141, 2080, 1489, 820, 1395, and 3040 individuals' baseline data were extracted from the 1997, 2000, 2004, 2006, 2009, and 2011 surveys, respectively. In this study, 191 participants with premature ASCVD and 114 participants with non-premature ASCVD (Supplementary Figure 1) were identified during a median follow-up of 9 years (range = 1-22 years). These 191 patients with premature ASCVD and 114 patients with non-premature ASCVD were matched with 573 and 342 non-ASCVD participants, respectively.

Baseline Characteristics

Participants with premature ASCVD and those without ASCVD did not differ on baseline characteristics, including marital status, smoking behavior, alcohol, tea, coffee, hypertension, diabetes, BMI, fat intake, protein intake, and WC. Compared with the non-ASCVD group, a higher proportion of the premature ASCVD participants had low levels of education (81.15% vs 59.58%, $P < .001$), had no medical insurance (70.16% vs 38.18%, $P < .001$), did not participate in physical activity (89.44% vs 81.18%, $P = .014$), resided in areas with low urbanization index (43.46% vs 16.93%, $P < .001$), had low levels of household income (40.00% vs 17.14%, $P < .001$), had high levels of energy intake (17.20% vs 10.85%, $P = .032$), and carbohydrate intake (44.07% vs 22.76%, $P < .001$) (Figure 1).

Similarly, compared with their non-ASCVD counterparts, the non-premature ASCVD participants had a higher proportion of individuals with a low level of education (90.00% vs 75.60%, $P = .002$), without medical insurance (77.19% vs 53.53%, $P < .001$), residing in areas with low urbanization index (49.12% vs 28.36%, $P < .001$), and having low household income (41.07% vs 26.41%, $P < .001$), high energy intake (26.17% vs 16.42%, $P = .035$), and carbohydrate intake (57.14% vs 35.99%, $P < .001$) (Supplementary Figure 2).

When compared with the non-premature ASCVD group, the premature ASCVD participants were more likely to be female (61.26% vs 36.84%, $P < .001$), non-drinkers (67.20% vs 50.00%, $P = .004$), and non-smoker (67.72% vs 51.75%, $P = .008$) (Figure 2).

Factors Associated With Premature ASCVD (Premature ASCVD vs non-ASCVD)

Based on the univariate analysis (Figure 1), when comparing the premature ASCVD participants with their non-ASCVD counterparts, history of hypertension, high energy intake, and high carbohydrate intake were significantly associated with increased risk of premature ASCVD, respectively; whereas, high levels of education or household income, having medical insurance, being unmarried (never married, divorced, widowed, and separated), overweight (vs underweight and/or normal weight), engaging in physical activity, and residing in areas with high urbanization were significantly associated with reduced risk of premature ASCVD ($P < .1$).

In multivariable analyses (Table 1), after adjusting for factors significantly associated with premature ASCVD risk in univariate analysis (P-values all $<.1$), hypertension disease history (adjusted hazard ratio [$HR_{adj.}$] = 1.68, 95% confidence interval [CI] = [1.14, 2.48]), obesity ($HR_{adj.}$ = 1.64, 95% CI = [1.03, 2.61]), and high level of carbohydrate intake ($HR_{adj.}$ = 1.46, 95% CI = [1.03, 2.08]) were independently associated with increased risk of premature ASCVD. Having medical insurance ($HR_{adj.}$ = 0.42, 95% CI = [0.28, 0.61]), living in areas with high urbanization index ($HR_{adj.}$ = 0.53, 95% CI = [0.33, 0.85]), with high level of household income ($HR_{adj.}$ = 0.48, 95% CI = [0.33, 0.71]) were independently associated with reduced risk of premature ASCVD.

Subgroup	No. of patients	Non-ASCVD (n = 573)	Premature ASCVD (n = 191)	HR$_{unadj.}$ (90%CI)	P value
Gender					
Male	276	202 (35.25)	74 (38.74)		
Female	488	371 (64.75)	117 (61.26)		
Age, y		45.18 (8.57)	45.50 (7.75)		
Education					
Primary education or less	494	339 (59.58)	155 (81.15)		
Secondary and tertiary education	266	230 (40.42)	36 (18.85)	0.42 (0.33−0.53)	<0.001
Medical insurance					
No	352	218 (38.18)	134 (70.16)		
Yes	410	353 (61.82)	57 (29.84)	0.29 (0.23−0.37)	<0.001
Marital status					
Married	693	515 (90.51)	178 (93.19)		
Unmarried	67	54 (9.49)	13 (6.81)	0.58 (0.38−0.90)	0.042
Drink					
No	502	375 (66.49)	127 (67.20)		
Yes	251	189 (33.51)	62 (32.80)	0.83 (0.67−1.03)	0.155
Smoke					
No	540	412 (72.15)	128 (67.72)		
Yes	220	159 (27.85)	61 (32.28)	1.18 (0.93−1.48)	0.255
Tea					
No	454	344 (60.14)	110 (57.59)		
Yes	309	228 (39.86)	81 (42.41)	1.03 (0.86−1.23)	0.764
Coffee					
No	727	541 (94.91)	186 (97.38)		
Yes	34	29 (5.09)	5 (2.62)	0.78 (0.49−1.25)	0.391
Physical activity					
No	614	453 (81.18)	161 (89.44)		
Yes	124	105 (18.82)	19 (10.56)	0.52 (0.38−0.70)	<0.001
Hypertension					
No	657	498 (87.37)	159 (83.25)		
Yes	104	72 (12.63)	32 (16.75)	1.32 (1.03−1.68)	0.061
Diabetes					
No	729	549 (96.83)	180 (95.74)		
Yes	26	18 (3.17)	8 (4.26)	1.29 (0.86−1.92)	0.303
BMI, kg/m²					
Normal (< 24)	350	256 (47.32)	94 (51.93)		
Overweight (≥ 24 and < 28)	271	209 (38.63)	62 (34.25)	0.82 (0.67−1.00)	0.094
Obesity (≥ 28)	101	76 (14.05)	25 (13.81)	1.11 (0.86−1.44)	0.505
Urbanization index					
Low (< 50)	180	97 (16.93)	83 (43.46)		
Middle (≥ 50 and < 75)	217	159 (27.75)	58 (30.37)	0.53 (0.42−0.67)	<0.001
High (≥ 75)	367	317 (55.32)	50 (26.18)	0.24 (0.18−0.32)	<0.001
Household income, yuan					
Low (≤ 3500)	173	97 (17.14)	76 (40.00)		
Middle (> 3500 and ≤ 8000)	240	170 (30.04)	70 (36.84)	0.62 (0.50−0.78)	<0.001
High (> 8000)	343	299 (52.83)	44 (23.16)	0.29 (0.23−0.37)	<0.001
Energy intake, kcal					
Normal (≤ 2800)	655	501 (89.15)	154 (82.80)		
High (> 2800)	93	61 (10.85)	32 (17.20)	1.42 (1.13−1.80)	0.013
Carbohydrate intake, g					
Normal (≤ 5.5*weight)	513	414 (77.24)	99 (55.93)		
High (> 5.5*weight)	200	122 (22.76)	78 (44.07)	2.15 (1.72−2.67)	<0.001
Fat intake, g					
Normal (≤ 1.15*weight)	421	317 (59.14)	104 (58.76)		
High (> 1.15*weight)	292	219 (40.86)	73 (41.24)	1.08 (0.90−1.29)	0.492
Protein intake, g					
Normal (≤ 1.8*weight)	687	520 (97.01)	167 (94.35)		
High (> 1.8*weight)	26	16 (2.99)	10 (5.65)	1.34 (0.91−1.96)	0.217
Waist circumference, cm					
Normal (male < 90 and female < 85)	460	345 (64.01)	115 (64.61)		
High (male ≥ 90 and female ≥ 85)	257	194 (35.99)	63 (35.39)	1.03 (0.85−1.24)	0.797

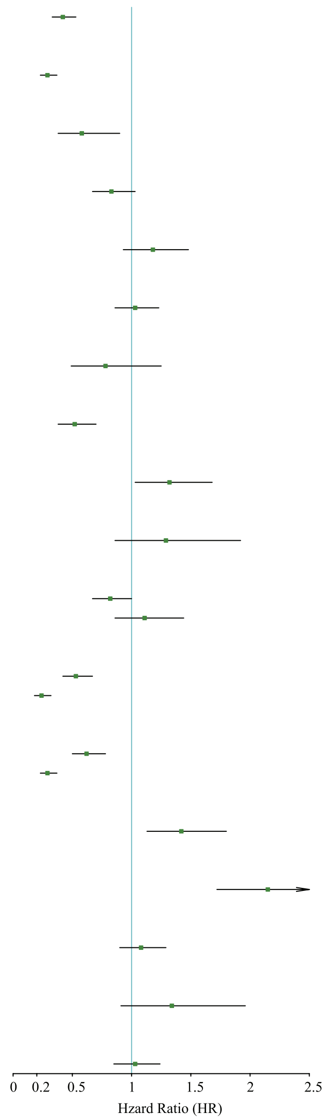

Figure 1. Baseline characteristics of non-ASCVD and premature ASCVD participants, and risk factors for premature ASCVD development based on univariate Cox regression analysis.[a]

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; CHNS, China Health and Nutrition Survey; CI, confidence interval; HR$_{adj.}$, adjusted hazard ratio.

[a]Each premature ASCVD case was matched with three non-ASCVD comparisons based on age, sex, and follow-up time. All values are presented as n (%) and mean ± standard deviation. Percentages may not total 100 because of rounding. Premature ASCVD was defined as having the first ASCVD event at age <55 years for men and <65 years for women.

Factors Associated With Non-Premature ASCVD (Non-Premature ASCVD vs Non-ASCVD)

As shown in Supplementary Figure 2, based on the univariate analysis results, participants with a high level of education, with medical insurance, lived in areas with high urbanization index, and with high household income were less likely to develop non-premature ASCVD. Those who reported a history of alcohol consumption and had high levels of energy or carbohydrate intake had a higher risk of non-premature ASCVD (each $P < .1$).

Based on the multivariable analysis, only the alcohol consumption and urbanization index of residence remained to be significant after adjusting for all other potential influencing

Subgroup	No. of patients	Non-premature ASCVD (n = 114)	Premature ASCVD (n = 191)	HR$_{unadj.}$ (90%CI)	*P* value
Gender					
Male	146	72 (63.16)	74 (38.74)		
Female	159	42 (36.84)	117 (61.26)	1.76 (1.38−2.25)	<0.001
Age, y		52.84 (6.58)	45.50 (7.75)	0.98 (0.97−1.00)	0.033
Education					
Primary education or less	254	99 (90.00)	155 (81.15)		
Secondary and tertiary education	47	11 (10.00)	36 (18.85)	1.44 (1.06−1.96)	0.048
Medical insurance					
No	222	88 (77.19)	134 (70.16)		
Yes	83	26 (22.81)	57 (29.84)	1.50 (1.15−1.94)	0.011
Marital status					
Married	278	100 (89.29)	178 (93.19)		
Unmarried	25	12 (10.71)	13 (6.81)	0.70 (0.43−1.13)	0.222
Drink					
No	184	57 (50.00)	127 (67.20)		
Yes	119	57 (50.00)	62 (32.80)	0.72 (0.56−0.93)	0.032
Smoke					
No	187	59 (51.75)	128 (67.72)		
Yes	116	55 (48.25)	61 (32.28)	0.63 (0.49−0.81)	0.003
Tea					
No	171	61 (53.51)	110 (57.59)		
Yes	134	53 (46.49)	81 (42.41)	0.98 (0.77−1.24)	0.874
Coffee					
No	299	113 (100.00)	186 (97.38)		
Yes	5	0 (0.00)	5 (2.62)		
Physical activity					
No	259	98 (91.59)	161 (89.44)		
Yes	28	9 (8.41)	19 (10.56)	1.33 (0.89−1.99)	0.24
Hypertension					
No	258	99 (87.61)	159 (83.25)		
Yes	46	14 (12.39)	32 (16.75)	1.91 (1.39−2.64)	0.001
Diabetes					
No	288	108 (95.58)	180 (95.74)		
Yes	13	5 (4.42)	8 (4.26)	2.61 (1.43−4.77)	0.009
BMI, kg/m²					
Normal (< 24)	150	56 (55.45)	94 (51.93)		
Overweight (≥ 24 and < 28)	99	37 (36.63)	62 (34.25)	1.26 (0.96−1.65)	0.171
Obesity (≥ 28)	33	8 (7.92)	25 (13.81)	2.46 (1.69−3.58)	<0.001
Urbanization index					
Low (< 50)	139	56 (49.12)	83 (43.46)		
Middle (≥ 50 and < 75)	98	40 (35.09)	58 (30.37)	1.12 (0.84−1.49)	0.506
High (≥ 75)	68	18 (15.79)	50 (26.18)	2.23 (1.65−3.02)	<0.001
Household income, yuan					
Low (≤ 3500)	122	46 (41.07)	76 (40.00)		
Middle (> 3500 and ≤ 8000)	111	41 (36.61)	70 (36.84)	1.00 (0.76−1.31)	0.977
High (> 8000)	69	25 (22.32)	44 (23.16)	1.47 (1.07−2.01)	0.045
Energy intake, kcal					
Normal (≤ 2800)	233	79 (73.83)	154 (82.80)		
High (> 2800)	60	28 (26.17)	32 (17.20)	0.66 (0.48−0.92)	0.037
Carbohydrate intake, g					
Normal (≤ 5.5*weight)	141	42 (42.86)	99 (55.93)		
High (> 5.5*weight)	134	56 (57.14)	78 (44.07)	0.59 (0.46−0.76)	0.001
Fat intake, g					
Normal (≤ 1.15*weight)	165	61 (62.24)	104 (58.76)		
High (> 1.15*weight)	110	37 (37.76)	73 (41.24)	1.29 (1.00−1.66)	0.094
Protein intake, g					
Normal (≤ 1.8*weight)	260	93 (94.90)	167 (94.35)		
High (> 1.8*weight)	15	5 (5.10)	10 (5.65)	0.88 (0.51−1.51)	0.696
Waist circumference, cm					
Normal (male < 90 and female < 85)	182	67 (67.00)	115 (64.61)		
High (male ≥ 90 and female ≥ 85)	96	33 (33.00)	63 (35.39)	1.44 (1.11−1.86)	0.022

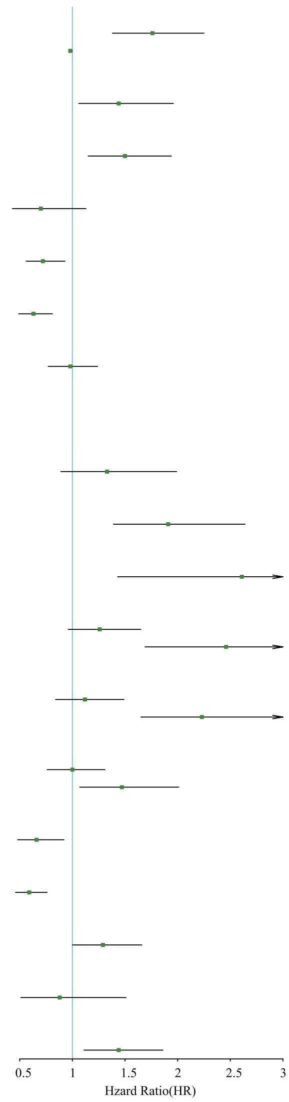

Figure 2. Baseline characteristics of premature ASCVD and non-premature ASCVD participants, and risk factors for earlier age of onset of ASCVD based on univariate Cox regression analysis.[a]

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; CHNS, China Health and Nutrition Survey; CI, confidence interval; HR$_{adj.}$, adjusted hazard ratio.

[a]All values are presented as n (%) and mean ± standard deviation. Percentages may not total 100 because of rounding. Stratified analyses for the risk factors for premature ASCVD development, in CHNS, using univariate Cox regression models. Premature ASCVD was defined as having the first ASCVD event at age <55 years for men and <65 years for women. Non-premature ASCVD was defined as having the first ASCVD event at age ≥55 years for men and ≥65 years for women.

factors that were significant in the univariate analysis. Alcohol consumption was independently associated with a 2.04-fold increased hazard of non-premature ASCVD (HR$_{adj.}$ = 2.04, 95% CI = [1.26, 3.28]); whereas participants residing in an area with high urbanization were less likely to have non-premature ASCVD (HR$_{adj.}$ = 0.37, 95% CI = [0.22, 0.62]) than their counterparts living in areas with low urbanization index (Table 1).

Factors Associated With the Advancement of the Onset Age of ASCVD (Premature ASCVD vs Non-Premature ASCVD)

When comparing the premature ASCVD group vs the non-premature ASCVD group, according to the univariate analysis result (Figure 2), risk factors of the early onset of ASCVD included a high level of education, medical insurance,

Table 1. Results of Three Multivariable Cox Proportional Hazards Regression Analyses.[a]

	Premature ASCVD vs non-ASCVD[b]		Non-premature ASCVD vs non-ASCVD[c]		Premature ASCVD vs non-premature ASCVD[d]	
Variable	$HR_{adj.}$ [95% CI]	*P*	$HR_{adj.}$ [95% CI]	*P*	$HR_{adj.}$ [95% CI]	*P*
Sex						
Male						
Female					1.59 [0.97, 2.60]	.067
Age (Years)					**0.96 [0.94, 0.98]**	**<.001**
Education						
Primary education or less						
Secondary and tertiary education	0.98 [0.66, 1.45]	.921	0.63 [0.35, 1.14]	.127	1.03 [0.64, 1.67]	.905
Medical insurance						
No						
Yes	**0.42 [0.28, 0.61]**	**<.001**	0.95 [0.63, 1.44]	.809	1.05 [0.68, 1.61]	.833
Marital status						
Married						
Unmarried	0.60 [0.32, 1.14]	.122				
Drink						
No						
Yes			**2.04 [1.26, 3.28]**	**.003**	0.95 [0.64, 1.42]	.801
Smoke						
No						
Yes					0.96 [0.60, 1.52]	.850
Tea						
No						
Yes						
Coffee						
No						
Yes						
Physical activity						
No						
Yes	0.73 [0.49, 1.10]	.129				
Hypertension						
No						
Yes	**1.68 [1.14, 2.48]**	**.009**			1.58 [0.99, 2.52]	.055
Diabetes						
No						
Yes					1.56 [0.70, 3.47]	.272
BMI						
BMI $<$ 24						
24 $\leq$ BMI $<$ 28	1.15 [0.84, 1.58]	.369			1.09 [0.73, 1.64]	.661
28 $\leq$ BMI	**1.64 [1.03, 2.61]**	**.037**			**2.08 [1.14, 3.80]**	**.017**
Urbanization index						
$<$ 50						
$\geq$ 50 and $<$ 75	0.84 [0.60, 1.20]	.341	0.84 [0.58, 1.22]	.367	1.33 [0.88, 1.99]	.173
$\geq$ 75	**0.53 [0.33, 0.85]**	**.008**	**0.37 [0.22, 0.62]**	**<.001**	**2.29 [1.33, 3.94]**	**.003**
Household income, yuan						
$\leq$ 3500						
$>$ 3500 and $\leq$ 8000	0.75 [0.54, 1.03]	.076	1.00 [0.66, 1.50]	.985	0.82 [0.55, 1.20]	.300
$>$ 8000	**0.48 [0.33, 0.71]**	**<.001**	0.73 [0.43, 1.23]	.240	1.33 [0.83, 2.12]	.235
Energy intake, kcal						
$\leq$ 2800						
$>$2800	1.13 [0.76, 1.68]	.537	1.11 [0.74, 1.65]	.613	0.81 [0.50, 1.30]	.376

(continued)

Table 1. (continued)

Variable	Premature ASCVD vs non-ASCVD[b]		Non-premature ASCVD vs non-ASCVD[c]		Premature ASCVD vs non-premature ASCVD[d]	
	$HR_{adj.}$ [95% CI]	*P*	$HR_{adj.}$ [95% CI]	*P*	$HR_{adj.}$ [95% CI]	*P*
Carbohydrate intake, g						
$\leq$ 5.5*weight						
$>$ 5.5*weight	**1.46 [1.03, 2.08]**	**.034**	1.38 [0.92, 2.06]	.119	1.02 [0.69, 1.50]	.939
Fat intake, g						
$\leq$1.15*weight						
$>$1.15*weight					1.28 [0.88, 1.87]	.192
Protein intake, g						
$\leq$1.8*weight						
$>$1.8*weight						
Waist circumference, cm						
Male $<$ 90 and female $<$ 85						
Male $\geq$ 90 and female $\geq$ 85					1.05 [0.68, 1.62]	.836

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; CI, confidence interval; HR, hazard ratio; SD, standard deviation.
[a]Hazard ratios were calculated using multivariable Cox proportional regression models.
[b]The multivariable-adjusted model was adjusted for factors with a $P < .1$ in univariate analysis, including educational level, medical insurance, marital status, physical activity, hypertension, BMI, urbanization index, household income, energy intake, and carbohydrate intake. Premature ASCVD was defined as having the first ASCVD event at age <55 years for men and <65 years for women.
[c]The multivariable-adjusted model was adjusted for factors with a $P < .1$ in univariate analysis, including educational level, medical insurance, alcohol consumption, urbanization index, household income, energy intake, and carbohydrate intake. Non-premature ASCVD was defined as having the first ASCVD event at age ≥55 years for men and ≥65 years for women.
[d]The multivariable-adjusted model was adjusted for factors with a $P < .1$ in univariate analysis, including sex, age, educational level, medical insurance, alcohol consumption, smoking, hypertension, diabetes, BMI, urbanization index, household income, energy intake, carbohydrate intake, fat intake, and waist circumference.

history of hypertension or diabetes, obesity, living in areas with high urbanization index, high household income, high fat intake, and high WC. In addition, women had a higher risk of early onset of ASCVD than men (each $P < .1$). However, older age, alcohol consumption, smoking, high energy intake, or high carbohydrate intake were statistically associated with reduced risk of early ASCVD onset.

After adjusting for all factors significantly associated with the risk of early onset of ASCVD in univariate analysis, obesity ($HR_{adj.}$ = 2.08, 95% CI = [1.14, 3.80]) and living in areas with high urbanization index ($HR_{adj.}$ = 2.29, 95% CI = [1.33, 3.94]) remained to be significantly and independently associated with increased risk of early onset of ASCVD.

Discussion

In this population-based longitudinal study, we explored possible risk factors for premature ASCVD among the Chinese population. Previous studies abroad[21] examined the relationship between common CVD risk factors (hypertension, obesity, etc.) as well as socioeconomic factors (education level, income level, etc.) and premature ASCVD. However, due to population heterogeneity, the effect of those factors may vary,[22] and the findings need to be further validated and re-evaluated in the Chinese population. Given the significantly higher loss of quality-adjusted life years among young patients with ASCVD, we aimed to explore the underlying risk factors to understand and mitigate the risk of incident premature ASCVD.

In our study, when comparing the premature ASCVD patients vs the non-ASCVD and non-premature ASCVD comparisons, hypertension was independently associated with increased risk of premature ASCVD, which was consistent with previous study findings.[15] Based on our adjusted analysis result, hypertensive participants had higher odds of premature ASCVD than non-premature ASCVD, although this association was not statistically significant (P = .055). Contrary to other studies, we did not find any significant association between hypertension and the risk of non-premature ASCVD. The association may be attributed to the duration of having hypertension rather than having a disease per se. With the trend toward the younger onset of hypertension and longer disease history,[23] the human body may be continuously exposed to hypertensive risk factors, significantly increasing the ASCVD prevalence and the risk of early onset in younger populations. As reported in prior studies, individuals with medical insurance tend to emphasize their health and be more proactive with disease prevention (eg, looking up health information online) than uninsured.[24] In our study, having medical insurance coverage may enable participants to detect risk factors and initiate preventive measures in a timely manner, ie, sooner for the younger population at risk for premature ASCVD.

We also found obesity had been independently associated with a higher risk of premature ASCVD when compared with both non-ASCVD and non-premature ASCVD participants. However, the association of obesity with the development of non-premature ASCVD was not significant based on the univariate analysis, suggesting BMI might be a risk factor for premature ASCVD but not for non-premature ASCVD. A previous study[25] found visceral obesity, but not subcutaneous adipose tissue, had been associated with CVD. Therefore, some researchers have suggested local body fat distribution index (such as WC) was more strongly associated with CVD outcomes than BMI,[26] because an increase in BMI resulted from an increase in subcutaneous or visceral adipose tissue (or both).[25-28] Although many studies suggested WC, which can reflect body fat distribution and upper body obesity, as a better indicator of cardiometabolic risk than BMI, this study did not find a significant association of WC with premature ASCVD. Since the distribution and composition of visceral adiposity at different ages may present different levels of ASCVD risk, our findings suggest for the younger population, BMI may be a better predictor of premature ASCVD than WC.

Another interesting finding was that living in areas with high urbanization index had been associated with decreased risk of premature and non-premature ASCVD, respectively. However, among individuals with ASCVD history, those living in areas with high urbanization index tended to experience ASCVD at a younger age. The urbanization index serves as a proxy for economic activity, population density, and health infrastructure.[29] Therefore, lower risk of ASCVD in areas with high urbanization index can be attributed to two aspects. At the individual level, people with superior socioeconomic status tend to have better educational backgrounds, leading to more healthy lifestyles. At the environmental level, more urban area usually has better health care access which can potentially improve the early detection of ASCVD risks or signs and prompt necessary preventive measures. However, for individuals with pre-existing risk of ASCVD, living in areas with a high level of urbanization corresponds with increased exposure to the unhealthy fast food-based diet, sedentary, unregulated work pattern, and high-pressure environment which may advance the progress of ASCVD development and making the ASCVD event to occur at an earlier age. In addition, advanced techniques of medical diagnosis in areas with high urbanization index may enable ASCVD diagnosis at earlier stage of disease development.

The adverse effects of smoking, drinking, and having diabetes on the development of ASCVD have been widely documented in previous studies.[11] A relatively high percentage of observations were missing information on these factors in our study, and we did not find significant associations. However, accounting for the duration of exposure to those risk factors might provide better insights into the effects of smoking, drinking, and having diabetes on ASCVD development.

Our study has several strengths. First, the CHNS program employed respondents with diverse socioeconomic and geographic backgrounds, enabling cross-socioeconomic comparisons and securing the representativeness of this study sample. Second, the use of the PSM method effectively mitigated the unbalanced data issue reducing selection bias while ensuring sufficient individual heterogeneity.

Among our study limitations are reliance on self-report of the ASCVD and other disease histories and defining cases as hypertensive based on measurement of their blood pressure on the same day. Current guidelines[30] recommend to identify hypertension cases using blood pressure values that are measured in different days. Furthermore, due to the lack of or incomplete information on other potential influencing factors (genetics, intensity and frequency of exercise, etc.), we were unable to access their effects on premature ASCVD.

Conclusion

In conclusion, in this longitudinal study, we revealed factors associated with premature ASCVD among the Chinese population. The effects of previously identified ASCVD risk factors may differ on the development and progression of premature ASCVD, suggesting that the intervention strategies for preventing premature ASCVD events need to be tailored accordingly. Future studies are warranted to further investigate the underlying pathological mechanisms given sufficient consideration of subpopulation biological and socioeconomic diversity.

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Author Contributions

YD, YZ, HH, and CC designed the study. YD performed the statistical analyses. YD and YZ drafted the manuscript. HH, CC, and YT revised the manuscript. CC had the primary responsibility for the final content. All authors read and approved the final manuscript.

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Data sets/Data Availability Statement

Data of the CHNS supporting the findings of this study are openly available at https://www.cpc.unc.edu/projects/china/data/datasets.

Supplemental Material

Supplemental material for this article is available online.

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