

# The Alternative Healthy Eating Index Is Associated with a Lower Risk of Fatal and Nonfatal Acute Myocardial Infarction in a Chinese Adult Population<sup>1–3</sup>

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## Abstract

**Background:** Indexes to quantify adherence to recommended dietary patterns have been developed for Western populations, but it is unclear whether these indexes can predict acute myocardial infarction (AMI) in Asian populations.

**Objectives:** We aimed to investigate the association between the Alternative Healthy Eating Index (AHEI)–2010 and risk of AMI and to evaluate potential mediation by traditional cardiovascular risk factors in a Chinese population.

**Methods:** A nested case-control study in 751 incident cases of AMI (564 nonfatal and 288 fatal) and 1443 matched controls was conducted within the prospective Singapore Chinese Health Study, a cohort of ethnic Chinese men and women aged 45–75 y. At baseline, habitual diet was assessed by using a validated, semiquantitative food-frequency questionnaire. AMI cases were ascertained via linkage with nationwide hospital databases (confirmed through medical record review) and the Singapore Birth and Death Registry. We evaluated the association between the AHEI-2010 and cardiovascular risk factors, including glycated hemoglobin, high-sensitivity C-reactive protein, creatinine, plasma lipids (LDL and HDL cholesterol, triglycerides), and blood pressure. ORs and 95% CIs were computed by using multivariable-adjusted conditional logistic regression models.

**Results:** Higher AHEI-2010 scores were associated with a lower risk of AMI (OR for the highest quartile compared with the lowest quartile: 0.62; 95% CI: 0.47, 0.81; *P*-trend < 0.001), with similar associations for fatal (OR: 0.60; 95% CI: 0.39, 0.94; *P*-trend = 0.009) and nonfatal (OR: 0.59; 95% CI: 0.43, 0.81; *P*-trend = 0.002) AMI. This association was only slightly attenuated after adjustment for potential biological intermediates (OR: 0.64; 95% CI: 0.48, 0.86; *P*-trend = 0.003).

**Conclusions:** Adherence to dietary recommendations as reflected in the AHEI-2010 was associated with a substantially lower risk of fatal and nonfatal AMI in an Asian population, and this association was largely independent of traditional cardiovascular risk factors. *J Nutr* 2016;146:1379–86.

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**Keywords:** Alternative Healthy Eating Index–2010, diet quality index, acute myocardial infarction, epidemiology, risk factors, nutrition

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## Introduction

Myocardial infarction is the leading cause of mortality worldwide (1), including in China and South East Asia (2). Diet is a key modifiable risk factor for the prevention of ischemic heart disease (3). Traditionally, nutritional epidemiology has focused largely on the investigation of single or a few nutrients or foods in relation to health outcomes, but the study of dietary patterns has emerged as a complementary approach that attempts to capture the impact of combinations of dietary exposures (4, 5).

Dietary patterns can be studied by using data-driven or hypothesis-driven methods (4, 5). Hypothesis-driven methods

define dietary patterns a priori on the basis of available evidence on the relation between a variety of foods and nutrients and health outcomes (6–10) and are used to examine the association between overall diet quality and chronic disease risk (4, 6, 7, 11). Examples of these dietary quality indexes include the DASH (Dietary Approaches to Stop Hypertension) diet (7), the Mediterranean diet (6, 8, 12), the Healthy Eating Index (10, 13, 14), and the Alternative Healthy Eating Index (AHEI)<sup>11</sup>–2010 (15). These dietary quality indexes were associated with a lower risk of cardiovascular diseases (CVDs) in Western populations (11, 15), but data for Asian populations are sparse. Dietary quality indexes

have primarily been developed on the basis of nutrition research in Western populations, and it remains unclear if these indexes can predict the risk of acute myocardial infarction (AMI) in Asian populations with different food consumption patterns. We therefore prospectively examined the association between adherence to the AHEI-2010 dietary quality index and the risk of AMI in participants of the Singapore Chinese Health Study (SCHS). We chose the AHEI-2010 index because it aims to capture the effects of diet on a variety of chronic diseases, is not population or cuisine specific, and aligns well with dietary guidelines in Singapore. We also examined the role of biological cardiovascular risk factors as potential mediators of the association between the AHEI-2010 and AMI risk.

## Methods

**Study population.** We used data from a nested case-control study conducted within a prospective cohort, the SCHS. The SCHS was established between April 1993 and December 1998 to evaluate the role of dietary and lifestyle factors in the development of chronic diseases in a Chinese population. The SCHS comprised 63,257 Chinese men and women of the Hokkein or Cantonese dialect groups who were aged 45–74 y at the time of recruitment. The SCHS participants were permanent residents or citizens of Singapore and were residing in government-built housing estates (~86% of Singaporeans lived in such residential estates) during the study enrollment (16). Self-reported information on demographic characteristics, lifestyle, and medical history were collected by using a structured interviewer-administered questionnaire (16, 17). This study was approved by the institutional review boards at the National University of Singapore and the University of Pittsburgh.

**Dietary assessment.** A validated, 165-item, semiquantitative FFQ designed specifically for the Singapore Chinese population was used to assess habitual dietary intakes of the study participants over the past year. The FFQ was administered through a face-to-face interview by trained interviewers in the participant's home. The frequency of consumption of each food item was determined by using 8 different frequency categories ranging from "never or hardly ever" to "two or more times a day" and 9 frequency categories for beverages, with the highest level being "six or more times a day." Three options for portion sizes were available for each food (16).

Energy and nutrient intakes for each participant were calculated by multiplying the frequency of consumption of each food by its energy or nutrient content and summing nutrient contributors across all of the food items and were estimated on the basis of the Singapore Food-Composition Database (16). The FFQ has been validated against two 24-h dietary recalls among 1022 randomly chosen SCHS cohort participants (16). This study showed correlations of 0.24 to 0.79 between FFQ and 24-h dietary recalls for energy and nutrients, similar to findings reported in other populations (18).

**Assessment of covariates and blood collection.** Self-reported information on demographic characteristics, height, weight, diet, moderate and vigorous physical activity, cigarette smoking, alcohol consumption, detailed menstrual and reproductive history (women only),

and medical history including physician-diagnosed hypertension, heart attack or angina, diabetes, and cancer were collected by using a structured interviewer-administered questionnaire at baseline (16, 17). Between July 1999 and June 2004 (follow-up 1), we attempted to re-contact all cohort participants and successfully re-interviewed 83% of the original cohort ( $n = 52,325$ ) by telephone to update their smoking status, alcohol consumption, medical history, and, for women, their menopausal status and use of replacement hormones.

Beginning in April 1994, blood and spot urine specimens were collected from a random 3% sample of study enrollees, and in January 2001 the accrual of biospecimens was extended to all surviving cohort members. By April 2005, biospecimens were collected from 60% of eligible cohort participants ( $n = 32,543$ ). Details on storage and processing of biospecimens were reported elsewhere (19).

Three blood pressure measurements were obtained from each participant, with a 3-min interval between measurements. Trained nurses measured systolic blood pressure (SBP) and diastolic blood pressure (DBP) according to standard procedures with the use of Omron automatic digital blood pressure monitors (HEM 705CP; Omron Healthcare) (20). The mean SBP and DBP of these 3 respective measurements were calculated and used for statistical analysis.

**Nested case-control study of AMI.** In our nested case-control study, we included SCHS cohort participants who provided blood samples and who were free of coronary artery disease and stroke at the time of blood collection according to self-reported medical history and information from the nationwide hospital discharge register.

Incident AMI cases were identified through electronic record linkages of the SCHS cohort database with a centralized, population-based Singapore Myocardial Infarction Registry or a nationwide hospital discharge database (1990–2010). Case verification through hospital discharge databases involved manual extraction of relevant clinical information from hospital records, and cases were subsequently verified by a consulting cardiologist by using the Multi-Ethnic Study of Atherosclerosis criteria for AMI (21). The fatal AMI cases were identified through the Singapore Registry of Births and Deaths [1993–2010; International Classification of Diseases (ICD) 9 codes 410–414]. Further details on the identification of cases have been previously described (22, 23). A total of 760 incident cases of fatal (ICD-9 codes 410–414) and nonfatal (ICD-9 code 410) AMI were identified.

For each of the 760 AMI cases, 2 healthy subjects were randomly selected as controls among all eligible cohort participants who were alive and free of coronary artery disease or stroke at the time of the AMI diagnosis of the index case by using an incidence-density sampling strategy (24). Controls were individually matched to the index case by sex, dialect group (Hokkein or Cantonese), year of birth ( $\pm 5$  y), date of enrollment ( $\pm 2.5$  y), and date of blood collection ( $\pm 6$  mo).

**Laboratory measurements of biomarkers.** Blood samples of case-control pairs were arranged in random order and were then analyzed at the National University Hospital Referral Laboratory in a blinded fashion. Biological cardiovascular risk factors including HDL cholesterol, LDL cholesterol (directly measured), TGs, high-sensitivity C-reactive protein (hsCRP), glycated hemoglobin (HbA1c), and creatinine were measured. HDL and LDL cholesterol and TGs were measured by using enzymatic (25) and colorimetric methods. hsCRP was analyzed by using a particle-enhanced immunoturbidimetric assay, and creatinine was measured by using creatininase. HbA1c was measured with the use of ion-exchange HPLC. HbA1c was measured in whole blood and the biomarkers were measured in plasma. The within-batch and between-batch CVs for the biomarkers were as follows: HDL cholesterol (0.65% and 3.53%), LDL cholesterol (1.38% and 4.17%), TGs (3.85 and 3.40%), hsCRP (2.25% and 3.53%), creatinine (1.05% and 1.75%), and HbA1c (0.99% and 1.02%).

**AHEI-2010.** The AHEI-2010 score was calculated on the basis of 10 of 11 components originally proposed by Chiuve et al. (15). *trans* Fat intake was not included as a component of the AHEI-2010 score in our study due to the lack of information on *trans* fat intake and low plasma *trans*

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<sup>3</sup> Supplemental Tables 1–3 are available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at <http://jn.nutrition.org>.

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<sup>11</sup> Abbreviations used: AHEI, Alternative Healthy Eating Index; AMI, acute myocardial infarction; CVD, cardiovascular disease; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin; hsCRP, high-sensitivity C-reactive protein; ICD, International Classification of Diseases; SBP, systolic blood pressure; SCHS, Singapore Chinese Health Study.

FA blood concentrations (median: 0.05% of total FAs; IQR: 0.03–0.06%) in our study population.

Higher scores were assigned for higher intakes of vegetables, fruit, whole grains, nuts and legumes, long-chain n–3 PUFAs, and PUFAs (% of energy). Lower scores were assigned for higher intakes of sodium, red meat, and sugar-sweetened beverages and fruit juice. The highest score was assigned to a moderate intake of alcohol and the lowest score was assigned to heavy intake. Each component score ranged from 0 (worst) to 10 (best), and the total AHEI-2010 score ranged from 0 (non-adherence) to 100 (highest adherence) on the basis of predetermined scoring criteria (15) (**Supplemental Table 1**). The original version of the AHEI was proposed by McCullough et al. (9).

For the vegetable score, we excluded potatoes and preserved vegetables; for the fruit score we excluded preserved or dried fruit; and for the nuts and legumes score we excluded sweetened soy products. We used 67 g (0.5 cup of typical local vegetables) to represent 1 serving for vegetables (15, 26), 16 g whole grains to represent 1 serving of whole-grain products (e.g., 1 slice of whole-wheat bread, 0.5 cup of oatmeal) (27), and 10 g to represent 1 serving of alcohol (26).

**Statistical analysis.** We excluded 32 participants (including 9 cases) who reported extreme energy intakes on the basis of predefined cutoffs for men (<700 or >3700 kcal/d) and women (<600 or >3000 kcal/d). We further excluded 17 matched controls due to the removal of the 9 cases and 4 controls due to insufficient plasma volume for the assessment of biomarkers. As a result, our analysis was based on 751 AMI cases (288 fatal and 564 nonfatal AMI) and 1443 matched controls. 101 participants developed AMI and died of fatal AMI. Hence, they were included in both fatal and nonfatal. There were 127 missing values for SBP that were imputed on the basis of a multiple linear regression equation that accounted for age, sex, and BMI (kg/m<sup>2</sup>). In addition, we accounted for LDL and HDL cholesterol in the regression model to impute 92 missing values for plasma TGs.

Partial correlation coefficients were computed for both the overall AHEI-2010 score and the individual AHEI-2010 component score with selected disease biomarkers, while controlling for potential confounders. The diet quality scores (AHEI-2010) were analyzed in quartiles on the basis of the distribution of the AHEI-2010 scores among control-group participants, with the lowest quartile as the reference category. Conditional logistic regression models were used to estimate ORs and 95% CIs of AMI associated with quartiles of AHEI-2010 scores and to adjust for potential confounders. We fitted 2 models with different sets of established and potential risk factors for AMI. In addition to main variable of interest (AHEI-2010 quartiles), the basic model included age at interview and total energy (kcal/d) in addition to conditioning on the matching factors including age ( $\pm 5$  y), sex (male or female), dialect group (Hokkein or Cantonese), year of interview (1993–1995 or 1996–1998), and date of blood collection ( $\pm 6$  mo). In the fully adjusted multivariate model, we further adjusted for level of education (none, primary school, or secondary school and above), cigarette smoking (never; ex-smoker; or current smoker: <13 or  $\geq 13$  cigarettes/d), physical activity (0 h/wk of moderate and strenuous activity, <4 h/wk of moderate activity or <2 h/wk of strenuous activity, or  $\geq 4$  h/wk of moderate activity or  $\geq 2$  h/wk of strenuous activity), BMI (<18.5, 18.5 to <23, 23 to <27.5, or  $\geq 27.5$ ), self-reported diabetes (yes or no), and hypertension (yes or no). We also conducted analyses of the AHEI-2010 score as a continuous variable per 10-point increment.

The potential interaction with the AHEI-2010 scores in relation to AMI risk was examined by including multiplicative interaction terms with current smoking (yes or no), BMI (<23 or  $\geq 23$ ), history of diabetes (yes or no), and hypertension (yes or no) in multivariable models. *P* values for trend were calculated by assigning the median value of the AHEI-2010 score in each quartile and modeling this as a continuous variable. We also conducted analyses stratified by sex. In addition, we examined associations between the individual components of AHEI-2010 and the risk of AMI per 2-point increment (the score for each AHEI-2010 component ranged from 0 to 10). Possible mediating effects of biological markers of CVD for the association between the AHEI-2010 and AMI risk were evaluated. Differences in the effect estimates derived from the multivariate models without and from those models with potential biological mediators were tested for significance (28).

We performed stepwise regression analysis to explore which food items or food groups had a considerable contribution to the variation in the AHEI-2010 score in our study population. This was done by modeling the AHEI-2010 score as a dependent variable and entering all food items assessed on the FFQ as independent variables among controls. All of the tests were 2-sided, and *P* < 0.05 was considered significant. Data were analyzed using STATA version 11.0 (StataCorp).

## Results

Mean  $\pm$  SD age was 59.5  $\pm$  7.9 y for AMI cases and 59.3  $\pm$  7.8 y for matched controls. Compared with controls, participants with AMI had a lower level of education, less physical activity, and a higher BMI and were more likely to smoke and to have a history of diabetes and hypertension. In addition, AMI cases had higher concentrations of LDL cholesterol, TGs, creatinine, HbA1c, hsCRP, and SBP and DBP and lower concentrations of HDL cholesterol than did controls (**Table 1**). Ninety-eight percent of women in the current study were postmenopausal at blood collection (i.e., the beginning of the follow-up for the incidence of fatal and nonfatal AMI). The dietary intakes of the AHEI-2010 food components and mean scores for cases and controls among Singapore Chinese adults in comparison with US study populations are shown in Supplemental Table 1. Compared with controls, participants with AMI had a lower overall AHEI-2010 score and lower scores for intakes of fruit, whole grains, nuts and legumes, long-chain n–3 PUFAs, PUFAs (representing low intake), alcohol (high or no intake), and red meat and sugar-sweetened beverages (high intake), although the difference was only significant for intakes of total fruit and long-chain n–3

**TABLE 1** Selected demographic characteristics of and risk factors for cases with AMI and controls<sup>1</sup>

Characteristics	Cases (n = 751)	Controls (n = 1443)	<i>P</i>
Baseline measurements			
Age at interview, y	59.5 $\pm$ 7.9	59.3 $\pm$ 7.8	Matched
Women, %	35.0	35.0	Matched
BMI, kg/m <sup>2</sup>	23.2 $\pm$ 3.1	22.9 $\pm$ 3.0	0.024
Higher education, <sup>2</sup> %	25.8	28.8	0.032
Current smoker, %	34.3	22.3	<0.001
Low physical activity, <sup>3</sup> %	74.0	67.6	0.009
History of hypertension, %	29.4	18.8	<0.001
History of diabetes, %	15.7	7.0	<0.001
Plasma concentrations			
LDL cholesterol, mmol/L	3.34 $\pm$ 0.87	3.18 $\pm$ 0.80	<0.001
HDL cholesterol, mmol/L	1.28 $\pm$ 0.30	1.34 $\pm$ 0.33	<0.001
TGs, mmol/L	1.67 $\pm$ 0.69	1.56 $\pm$ 0.67	<0.001
HbA1c, %	6.64 $\pm$ 1.63	6.14 $\pm$ 1.13	<0.001
hsCRP, <sup>4</sup> mg/L	1.5 (0.7, 3.5)	1.0 (0.5, 2.3)	<0.001
Creatinine, $\mu$ mol/L	77.17 $\pm$ 56.63	69.96 $\pm$ 29.39	0.001
Blood pressure measurements, mm Hg			
Systolic blood pressure	149.3 $\pm$ 24.3	140.2 $\pm$ 21.5	<0.001
Diastolic blood pressure	83.4 $\pm$ 14.2	80.7 $\pm$ 10.4	<0.001

<sup>1</sup> Values are means  $\pm$  SDs for continuous variables and percentages for categorical variables unless otherwise indicated. *P* values were estimated on the basis of univariate conditional logistic regression. AMI, acute myocardial infarction; HbA1c, glycated hemoglobin; hsCRP, high-sensitivity C-reactive protein.

<sup>2</sup> Secondary school and above.

<sup>3</sup> 0 h/wk of moderate and strenuous activity.

<sup>4</sup> Values are medians (25th, 75th percentiles).

PUFAs. We compared the AHEI-2010 score and its components in our study population with that observed in US populations. We did not observe major differences in scores for fruit, PUFAs, and sodium. However, vegetable and alcohol intakes were lower in our study population than in the US populations. Due to higher intakes of fish and soy products and lower intakes of red meat and sugar-sweetened beverages among Singapore Chinese, we observed higher scores for long-chain n-3 PUFAs and legumes and lower scores for red meat and sugar-sweetened beverages than in US populations. The mean AHEI-2010 score among our participants was higher than that of their US counterparts. The distributions of established risk factors for AMI according to quartile of the AHEI-2010 score among controls are shown in Table 2. Participants with a higher AHEI-2010 score were more likely to be women but less likely to be current smokers, had a higher level of education, and a higher frequency of physical exercise.

Table 3 shows the partial correlations between the overall AHEI-2010 score and individual component scores at baseline with biological markers that are associated with risk of AMI, which were measured, on average, 6.6 y apart. The overall

AHEI-2010 score was not associated with any of the risk biomarkers measured, including LDL and HDL cholesterol, TGs, HbA1c, hsCRP, creatinine, and SBP and DBP. A higher vegetable score was significantly correlated with lower blood pressure; a higher alcohol score (reflecting moderate intake) with higher HDL cholesterol; a higher whole-grain intake with lower LDL cholesterol, TGs, and DBP; a higher long-chain n-3 PUFA intake with higher LDL cholesterol and lower SBP; and a higher sodium score (reflecting lower intakes) with lower hsCRP. No significant association was found for components of the AHEI-2010 scores with other biological risk markers or blood pressure.

The association between the AHEI-2010 score and risk of AMI is shown in Table 4. Compared with the lowest quartile, ORs (95% CIs) of total, fatal, and nonfatal AMI for the highest AHEI-2010 score were 0.62 (0.47, 0.81), 0.60 (0.39, 0.94), and 0.59 (0.43, 0.81), respectively, after adjustment for age, sex, BMI, level of education, smoking, physical inactivity, and history of diabetes and hypertension (all *P*-trend < 0.001). We did not observe a significant effect modification by sex, smoking status, BMI, history of previous diabetes, and hypertension

**TABLE 2** Distribution of risk factors for AMI according to quartile of the AHEI-2010 score among controls<sup>1</sup>

Characteristics	Quartile of AHEI-2010 score				<i>P</i> -trend <sup>2</sup>
	1 ( <i>n</i> = 360)	2 ( <i>n</i> = 361)	3 ( <i>n</i> = 361)	4 ( <i>n</i> = 361)	
AHEI-2010 score <sup>3</sup> (possible range: 0–100)	42 (21–45)	48 (46–50)	53 (50–55)	59 (55–81)	<0.001
Baseline measurements					
Age at interview, y	59.1 ± 7.9	59.1 ± 7.6	59.8 ± 7.9	59.4 ± 7.7	0.46
Women, %	28.6	33.8	39.6	38.8	0.002
BMI, kg/m <sup>2</sup>	22.7 ± 3.0	22.9 ± 3.1	22.9 ± 3.0	22.9 ± 2.8	0.43
Higher education (at least secondary school), <sup>4</sup> %	22.8	26.9	27.7	37.7	<0.001
Current smoker, %	27.2	24.1	21.0	16.9	0.001
Low physical activity, <sup>5</sup> %	76.1	69.8	63.4	60.9	<0.001
History of hypertension, %	16.4	20.5	17.2	21.3	0.14
History of diabetes, %	6.4	6.4	6.4	8.9	0.20
Components of AHEI-2010					
Vegetables, <sup>6</sup> servings/d	1.1 ± 0.5	1.3 ± 0.6	1.4 ± 0.7	2.0 ± 1.0	<0.001
Fruit, <sup>7</sup> servings/d	0.7 ± 0.6	1.1 ± 0.8	1.4 ± 1.0	2.0 ± 1.3	<0.001
Whole grains, g/d	2.9 ± 7.0	4.2 ± 9.6	8.3 ± 13.6	12.8 ± 17.2	<0.001
Nuts and legumes, <sup>8</sup> servings/d	0.3 ± 0.3	0.5 ± 0.4	0.7 ± 0.4	1.1 ± 0.7	<0.001
Moderate alcohol intake, <sup>9</sup> %	1.1	3.6	6.7	11.6	<0.001
Long-chain n-3 PUFAs, mg/d	273 ± 196	314 ± 168	353 ± 159	394 ± 219	<0.001
PUFAs, % of energy	4.0 ± 1.2	4.7 ± 1.4	5.2 ± 1.7	6.4 ± 2.2	<0.001
Sugar-sweetened beverage and juice intake, <sup>10</sup> % with ≥1 serving/d	11.4	2.5	1.1	0.8	<0.001
Red and processed meat intake, <sup>11</sup> servings/d	0.38 ± 0.28	0.32 ± 0.22	0.30 ± 0.22	0.27 ± 0.20	<0.001
Sodium intake, mg/d	1170 ± 619	1110 ± 556	1070 ± 492	1130 ± 533	0.34

<sup>1</sup> Values are means ± SDs unless otherwise indicated; percentages are based on nonmissing data. AHEI, Alternative Healthy Eating Index; AMI, acute myocardial infarction.

<sup>2</sup> Calculated by assigning the median value of AHEI-2010 score in each quartile and modeling this as a continuous variable in separate regression models with each characteristic as the outcome.

<sup>3</sup> Values are medians; ranges in parentheses.

<sup>4</sup> Secondary school and above.

<sup>5</sup> 0 h/wk of moderate and strenuous activity.

<sup>6</sup> One serving = 67 g (0.5 cup of typical local vegetables).

<sup>7</sup> One serving = 1 medium piece of fruit.

<sup>8</sup> One serving = 1 medium-size tofu item or 1 tablespoon of peanut butter.

<sup>9</sup> 0.5–1.5 drinks/d for women and 0.5–2.0 drinks/d for men; 1 serving of alcohol = 10 g.

<sup>10</sup> One serving = 1 glass, packet, or typical local portion of sugar-sweetened beverage or fruit juice.

<sup>11</sup> One serving = 113.4 g unprocessed meat or 42.5 g processed meat.

**TABLE 3** Partial correlations of the AHEI-2010 score and food groups included in the score with biological risk factors for CVD measured, on average, 6–7 y after dietary assessment among 2084 participants<sup>1</sup>

Components of AHEI-2010	Biological risk factors							
	LDL-C (n = 1743) <sup>2</sup>	HDL-C (n = 1743) <sup>2</sup>	TGs (n = 1743) <sup>2</sup>	HbA1c (n = 1743) <sup>2</sup>	hsCRP (n = 1743) <sup>2</sup>	Creatinine (n = 1743) <sup>2</sup>	SBP (n = 1122) <sup>3</sup>	DBP (n = 1122) <sup>3</sup>
AHEI-2010 score	−0.024	0.029	−0.036	−0.015	−0.014	−0.011	−0.058	−0.053
Vegetables	−0.009	−0.040	−0.020	−0.023	0.019	0.019	−0.077*	−0.089**
Fruit	−0.004	−0.008	−0.016	0.034	−0.009	−0.027	−0.042	0.003
Whole grains	−0.063**	0.038	−0.065**	−0.005	−0.023	−0.004	−0.055	−0.085**
Nuts and legumes	−0.011	−0.010	−0.007	−0.022	0.022	0.007	−0.047	−0.045
Alcohol	0.042	0.096***	0.022	−0.016	−0.010	−0.040	0.055	0.041
Long-chain n–3 PUFAs	0.063**	−0.004	0.017	0.037	0.034	0.007	−0.011	0.002
PUFAs, % of energy	−0.015	0.009	−0.023	−0.009	0.021	−0.005	−0.072*	−0.049
Low sugar-sweetened beverage and juice intake	−0.043	0.024	−0.032	−0.042	−0.023	0.029	−0.025	−0.033
Low red and processed meat intake	−0.044	0.004	−0.023	−0.019	−0.043	−0.006	−0.011	0.015
Low sodium intake	−0.039	−0.008	−0.014	0.008	−0.065**	−0.022	0.048	0.034

<sup>1</sup> The mean  $\pm$  SD time after dietary assessment was 6.6  $\pm$  1.9 y. Duplicate controls were excluded. TGs, HbA1c, hsCRP, and creatinine were log-transformed. \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ . AHEI, Alternative Healthy Eating Index; CVD, cardiovascular disease; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin; HDL-C, HDL cholesterol; hsCRP, high-sensitivity C-reactive protein; LDL-C, LDL cholesterol; SBP, systolic blood pressure.

<sup>2</sup> Correlations were adjusted for disease status (case or control), age at interview (y), sex (male or female), dialect group (Hokkien or Cantonese), year of interview (1993–1995 or 1996–1998), year blood was collected, total energy intake (kcal/d), level of education (none, primary, or secondary and above), cigarette smoking (never; ex-smoker; current smoker:  $<13$  or  $\geq 13$  cigarettes/d), physical activity (0 h/wk of moderate and strenuous activity,  $<4$  h/wk of moderate or  $<2$  h/wk of strenuous activity,  $\geq 4$  h/wk of moderate or  $\geq 2$  h/wk of strenuous activity), BMI (kg/m<sup>2</sup>;  $<18.5$ , 18.5 to  $<23$ , 23 to  $<27.5$ , or  $\geq 27.5$ ), with the exclusion of 341 participants with a history of physician-diagnosed diabetes.

<sup>3</sup> Correlations were adjusted as in footnote 2, with further exclusion of 621 participants with a history of physician-diagnosed hypertension.

(Supplemental Table 2). Adjustment for traditional biological risk factors, including blood pressure, plasma lipids, hsCRP, creatinine, and HbA1c, only slightly attenuated the association between the AHEI-2010 and AMI risk. On the basis of the analysis modeling AHEI-2010 as a continuous variable, adjustment for these biological risk factors explained 15.5% of the association for total AMI and 18.3% for nonfatal AMI risk and 0% for fatal AMI risk (Table 4).

Individual components of the AHEI-2010 that were independently associated with a lower risk of AMI included higher intakes of fruit and long-chain n–3 PUFAs and lower intakes of red and processed meat and sugar-sweetened beverages and fruit juice. A higher intake of fruit and PUFAs and a moderate intake of alcohol also were associated with a lower risk of AMI, but these associations were not significant after adjustment for other risk factors for AMI (Supplemental Table 3).

To provide insight into the specific foods that contributed to the AHEI-2010, we identified individual foods that explained the maximum variation in the score. Of the 165 food items, the top 20 foods explained 62% of variance in the AHEI-2010 score. Among these 20 foods, several soy foods (plain tofu in soups, *Yong tau foo*, *tau kwa*), boiled or steamed fish, peanut butter, nuts, several fruits (oranges, bananas, and papaya) and vegetables (onion, *po choy*, pak choy), whole-wheat bread, and hot oats and other hot cereals were associated with a higher score. In contrast, soft drinks, orange juice, flavored rice, fried rice, pork belly, and milk were associated with a lower score.

## Discussion

In this nested case-control study, we observed an inverse association between the AHEI-2010 dietary quality index and the risk of AMI in the Singapore Chinese population, with an  $\sim 40\%$  lower AMI risk for the highest compared with the lowest quartile. This association was similar for fatal and nonfatal AMI

and was observed in both men and women. In analyses of individual components of the AHEI-2010, higher intakes of long-chain n–3 fatty acids and lower intakes of sugar-sweetened beverages and juices were significantly associated with a lower AMI risk after adjusting for potential confounders.

Our study results are comparable to evidence from other studies conducted in Western populations, in which adherence to the AHEI-2010 was inversely associated with the risk of coronary heart disease (15), CVD mortality (11), and total mortality in patients with myocardial infarction (29). In the Health Professionals Follow-Up Study and the Nurses' Health Study, comparing the highest quintile with the lowest quintile of the AHEI-2010 was associated with a 31% lower risk of major coronary heart disease (15). Observational studies conducted in postmenopausal women (11) and a multiethnic population (30) in the United States showed an  $\sim 20\%$  lower risk of CVD mortality in the highest compared with the lowest quintile of the AHEI-2010. A recent study conducted in Shanghai in Chinese women and men also showed a 30–40% lower risk of CVD mortality in the highest quartile of the modified AHEI-2010 (31). However, that study did not include whole grains, sugar-sweetened beverages, and *trans* fat in the originally proposed AHEI-2010.

Consistent with other studies, our study supports a beneficial effect of whole grains (32–34) and moderate alcohol intake (35–37) on plasma lipid profiles. Similar to other studies, our study found a higher sodium intake with higher plasma hsCRP (38) and a higher intake of PUFAs was associated with lower SBP (39). In contrast with these individual AHEI-2010 components, the overall AHEI-2010 was not significantly associated with CVD biomarkers. In previous studies, dietary quality indexes were associated with more favorable values of markers of inflammation and endothelial dysfunction (40), hsCRP (41, 42), serum insulin (42), SBP (41), and total (41) and HDL (42) cholesterol. The longer duration between self-reported diet at baseline and biospecimen collection might have explained the

**TABLE 4** ORs (95% CIs) of fatal and nonfatal AMI by quartile of the AHEI-2010 in Singapore Chinese Health Study participants<sup>1</sup>

	Quartile of AHEI-2010 score				P-trend <sup>2</sup>	AHEI-2010 score (per 10 points)
	1 (lowest)	2	3	4 (highest)		
Median score (IQR)	42 (39–44)	48 (47–49)	53 (51–54)	59 (57–62)		
Overall						
Cases/controls, <i>n</i>	241/360	198/361	169/361	143/361		751/1443
Basic model <sup>3</sup>	1.0 (ref)	0.83 (0.66, 1.06)	0.71 (0.55, 0.90)	0.59 (0.46, 0.76)	< 0.001	0.77 (0.68, 0.86)
Full model <sup>4</sup>	1.0 (ref)	0.84 (0.66, 1.08)	0.75 (0.58, 0.98)	0.62 (0.47, 0.81)	< 0.001	0.79 (0.70, 0.90)
Full model + intermediates <sup>5</sup>	1.0 (ref)	0.80 (0.61, 1.04)	0.75 (0.57, 0.99)	0.64 (0.48, 0.86)	0.003	0.82 (0.72, 0.94)
Change, <sup>6</sup> %	—	—	—	—		15.5
Fatal AMI						
Cases/controls, <i>n</i>	98/142	78/128	57/143	55/138		288/551
Basic model <sup>3</sup>	1.0 (ref)	0.91 (0.62, 1.33)	0.59 (0.40, 0.88)	0.59 (0.40, 0.89)	0.003	0.78 (0.64, 0.94)
Full model <sup>4</sup>	1.0 (ref)	0.94 (0.62, 1.43)	0.60 (0.39, 0.93)	0.60 (0.39, 0.94)	0.009	0.78 (0.64, 0.96)
Full model + intermediates <sup>5</sup>	1.0 (ref)	0.92 (0.59, 1.44)	0.62 (0.39, 0.98)	0.58 (0.36, 0.94)	0.011	0.78 (0.63, 0.98)
Change, <sup>6</sup> %	—	—	—	—		0
Nonfatal AMI						
Cases/controls, <i>n</i>	182/279	146/271	132/268	104/265		564/1083
Basic model <sup>3</sup>	1.0 (ref)	0.85 (0.64, 1.11)	0.77 (0.58, 1.01)	0.59 (0.44, 0.80)	0.001	0.76 (0.66, 0.87)
Full model <sup>4</sup>	1.0 (ref)	0.85 (0.64, 1.14)	0.83 (0.61, 1.11)	0.59 (0.43, 0.81)	0.002	0.77 (0.66, 0.90)
Full model + intermediates <sup>5</sup>	1.0 (ref)	0.79 (0.58, 1.07)	0.83 (0.60, 1.13)	0.64 (0.45, 0.90)	0.016	0.81 (0.69, 0.95)
Change, <sup>6</sup> %	—	—	—	—		18.3

<sup>1</sup> AHEI, Alternative Healthy Eating Index; AMI, acute myocardial infarction; ref, reference.

<sup>2</sup> Calculated by assigning the median value of the AHEI-2010 score in each quartile and modeling this as a continuous variable in models.

<sup>3</sup> Covariates adjusted for through matching included age ( $\pm 5$  y) at biospecimen collection, sex (male or female), dialect group (Hokkien or Cantonese), year of interview (1993–1995 or 1996–1998), and year blood was collected. In addition, we adjusted for age at interview (y) and total energy intake (kcal/d).

<sup>4</sup> In addition to the basic model, we adjusted for level of education (none, primary, or secondary and above), cigarette smoking (never; ex-smoker; current smoker:  $< 13$  or  $\geq 13$  cigarettes/d), physical activity (0 h/wk of moderate and strenuous activity,  $< 4$  h/wk of moderate or  $< 2$  h/wk of strenuous activity,  $\geq 4$  h/wk of moderate or  $\geq 2$  h/wk of strenuous activity), BMI ( $\text{kg}/\text{m}^2$ ;  $< 18.5$ , 18.5 to  $< 23$ , 23 to  $< 27.5$ , or  $\geq 27.5$ ), history of diabetes (yes or no), and history of hypertension (yes or no).

<sup>5</sup> In addition to the full model, we further adjusted for LDL and HDL cholesterol, TGs, high-sensitivity C-reactive protein, glycated hemoglobin, creatinine, and systolic blood pressure.

<sup>6</sup> Percentage change in regression coefficients as a result of adjustment for potential intermediates.

null associations between the AHEI-2010 score and biological markers of AMI risk in our study.

In the analyses of biological intermediates of CVD risk, the PREDIMED (Prevención con Dieta Mediterránea) study (43) showed beneficial effects of the Mediterranean diet on blood pressure, plasma lipid profiles, and inflammation. In our study, the association between AHEI-2010 and AMI risk appeared to be largely independent of traditional biological risk factors for CVDs. However, the putative cardioprotective role of higher scores on the AHEI-2010 could possibly be explained by other biological mediators such as arrhythmia, thrombosis, and insulin resistance. For example, phytochemicals (e.g., anti-inflammatory and insulin-sensitizing properties) and dietary *n*-3 PUFAs (e.g., antiarrhythmic properties) may offer protection against heart disease through these alternative biological pathways (44, 45).

Strengths of our study include the ascertainment of both fatal and nonfatal AMI, the prospective study design with dietary assessment and blood collection before the start of disease follow-up, which minimizes the likelihood of recall and selection bias. Several potential limitations of our study should also be considered. Although we observed reasonable agreement between nutrients assessed with the FFQ and 24-h recalls, some amount of measurement error in the dietary assessment is

inevitable. As with most other FFQs, our FFQ did not accurately capture discretionary salt use in cooking or at the table and the results for the sodium component of the AHEI-2010 should be interpreted with caution. We did not include the originally proposed *trans* fat component in the calculation of the AHEI-2010 due to the lack of information on *trans* fat intake in our study population. However, the extremely low concentrations of plasma *trans* fats in our study population relative to US populations (15, 46) suggest a minimal impact of *trans* fat on the AHEI-2010 score in our analysis. In addition, dietary assessment was done only at baseline and dietary changes during follow-up were not recorded. However, due to the prospective design, any subsequent change in diet would likely lead to nondifferential misclassification and potentially attenuate the association with AMI risk. Finally, as in all observational studies, we cannot exclude the possibility that measurement error in the assessment of confounders or lack of control for other confounders may have contributed to the observed associations.

In conclusion, our study findings suggest that higher adherence to dietary recommendations as reflected in the AHEI-2010 was associated with a substantially lower risk of nonfatal and fatal AMI in Singapore Chinese. The specific foods that characterized a high AHEI-2010 diet quality score are different

for Chinese than for Western populations. Given the strong inverse association between the AHEI-2010 score and AMI risk, broader food groups and nutrients encompassed within the AHEI-2010 can be recommended to Chinese and possibly other Asian populations. Our findings thus support the promotion of a healthy eating pattern high in plant foods (fruit and vegetables, nuts and legumes, and whole grains) and healthy sources of fat (long-chain n-3 PUFAs and total PUFAs) with a moderate intake of alcohol and low intakes of sodium, red and processed meat, and sugar-sweetened beverages for lowering the incidence of myocardial infarction in Chinese populations.

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