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Association of ideal cardiovascular health metrics with serum uric acid, inflammation and atherogenic index of plasma: A population-based survey

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HIGHLIGHTS

- The link between inflammatory score, serum uric acid (SUA) and atherogenic index of plasma (AIP) with cardiovascular health (CVH) score was evaluated.
- A negative association between SUA and CVH score was observed.
- AIP was inversely related to CVH score.
- Significant reductions in the odds of "high-risk atherosclerosis" and "CVD risk" were found across CVH categories.

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ABSTRACT

Background and aims: We aimed to evaluate the link between inflammatory score [consisting of C-reactive protein (CRP) and white blood cells], serum uric acid (SUA) and atherogenic index of plasma (AIP) and the cardiovascular health (CVH) score.

Methods: We used the cross-sectional National Health and Nutrition Examination Survey database. Statistical analyses accounted for the survey design and sample weights.

Results: Overall, there were 23,004 participants (mean age = 47.2 years, 46.5% males). Participants with an ideal CVH level had the highest ratio of poverty to income (3.62%, $p < 0.001$), as well as lower levels of CRP, SUA and AIP ($p < 0.001$ for all comparisons). In adjusted linear regression, a significant negative association was observed between inflammatory score ($\beta = -0.052$, $p < 0.001$), SUA ($\beta = -0.041$, $p < 0.001$) and AIP ($\beta = -0.039$, $p < 0.001$) and CVH score, i.e. participants with a better (greater) CVH score had a lower inflammatory score. Results from adjusted logistic regression showed reduction in the likelihood of "high-risk atherosclerosis" (defined as AIP ≥ 0.21) [intermediate: odds ratio (OR) = 0.90, 95% confidence interval (CI):0.85–0.95, ideal: OR = 0.81, 95%CI: 0.74–0.88] and "high CVD risk" (defined as CRP ≥ 3 mg/l) [intermediate: OR = 0.86, 95%CI:0.73–0.98, ideal: OR = 0.82, 95%CI:0.69–0.95] across the categories of CVH.

Conclusions: Our findings highlight that CVH metrics were associated with inflammatory score, SUA and AIP. Furthermore, participants with a better CVH score had a lower CVD risk. These results reinforce the importance of implementing healthy behaviours as proposed by the American Heart Association. If confirmed in clinical trials, this knowledge may have implications for CVD prevention and management.

1. Introduction

Evidence suggests that inflammation plays a key role in the pathogenesis of cardiovascular diseases (CVD) [1]. C-reactive protein (CRP) is an acute-phase protein produced by hepatocytes in response to inflammatory cytokines such as interleukin-6 (IL-6) [1]. Circulating markers of inflammation, including CRP, tumour necrosis factor-α (TNF-α) and some interleukins (IL-6 and IL-1), have been associated

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with the risk of CVD [1]. Furthermore, plasma CRP may be a predictor of both CVD and type 2 diabetes (T2D) [1]. However, it has also been reported that CRP is not always associated with diagnosed CVD when compared with some more precise and invasive techniques [2].

A score that combines several inflammatory biomarkers could provide an overall estimation of the inflammatory status. In this regard, white blood cells (WBCs) may provide a better index of inflammation together with CRP [3]. WBCs are considered as a reliable biomarker of inflammation and might also represent a cardio-metabolic factor that could predict CVD [4]. Therefore, both CRP and WBCs could be predictors of CVD events and mortality. They could also be used to monitor cardio-metabolic health status.

Several studies have shown that hyperuricaemia is linked to CVD, hypertension, metabolic syndrome (MetS), kidney failure and T2D [5–9]. Serum uric acid (SUA) may play an important role in metabolic, homeostatic and haemodynamic abnormalities, such as insulin resistance, abdominal obesity, and dyslipidaemia; several studies indicated SUA as a component of the MetS [10].

The atherogenic index of plasma (AIP) has been suggested as a risk factor for CVD and it was shown to be a significant predictor of atherosclerosis better than low density lipoprotein cholesterol (LDL-C) levels [11,12]. AIP is calculated as the log ratio of triglycerides (TG) to high-density lipoprotein cholesterol (HDL-C) levels [11]. After the logarithmical transformation, the AIP could correct for the lack of normal distribution and demonstrate a correlation with smaller LDL particles and increased fractional esterification rate [11,12]. Apart from atherosclerosis, the AIP was also significantly related to acute coronary syndromes (ACS) [12], CVD and its risk factors [11,12]. Taken together, both SUA and AIP are indicators of cardio-metabolic health status.

In 2010, the American Heart Association (AHA) suggested the ideal cardiovascular health index (ICHI) [13]. The main aim was to reduce CVD mortality by 20% and improve cardiovascular health (CVH) by 20% by 2020 and beyond [13]. These recommendations included 4 health behaviours and 3 health factors. The behaviour criteria were non-smoking, physical activity, normal body mass index (BMI), and healthy diet, whereas the health factors included normal blood pressure (BP), plasma total cholesterol and glucose. Achieving a greater number of ideal CVH metrics has been associated with a lower risk for CVD events and mortality [14]. Therefore, the ICHI could represent a useful epidemiological tool to assess CVD risk.

With regard to inflammation, a study of 543 adolescents including 251 boys and 292 girls from the Healthy Lifestyle in Europe by Nutrition in Adolescence (HELENA), reported that a higher CVH was associated with a lower inflammatory score, as well as with several individual components of CVH, both in boys and girls [15]. Another cross-sectional study among Chinese adults also reported a reverse link between CRP and CVH score [16]. To the best of our knowledge, there is no study evaluating the association between SUA and CVH metrics. With regard to AIP, there are only two studies available in Chinese populations [1718]; both reported that CVH metrics significantly correlated with AIP. Overall, uncertainty remains regarding the relationship between ideal CVH metrics and AIP due to the limited studies in general populations.

Considering the potentially unique utility of the AIP as an independent marker of CVD risk, and the relatively limited available data evaluating the AIP as an outcome, the present study was designed to assess the AIP as an outcome of interest. Given that CVD mortality is increasing in the USA [19], accounting for 864,000 deaths annually, we aimed to evaluate the association of ideal CVH metrics with inflammatory score, SUA and AIP. Furthermore, we estimated the likelihood of CVD risk according to CVH metrics. We hypothesized that subjects with a higher CVH score (protective profile) have a more favourable inflammatory score, SUA, AIP and a lower risk of CVD events. The reason for choosing the inflammatory score, SUA and AIP is that they have been used as alternative indicators of CVD events and mortality and they might play a role as important components in CVH metrics.

2. Materials and methods

2.1. Population characteristics

The National Health and Nutrition Examination Survey (NHANES, cross-sectional) conducted by the US National Center for Health Statistics (NCHS) [20]. NHANES uses a complex, multistage and stratified sampling design to select a representative sample of the civilian and non-institutionalized resident population of the USA [20]. The NCHS Research Ethics Review Board approved the NHANES protocol and consent was obtained from all participants [20]. The current study was based on analysis of data collected from 2005 to 2010. Data collection on demographics occurs through in-home administered questionnaires, while anthropometric and biochemistry data are collected by trained personnel using mobile exam centres. More detailed information is available elsewhere [20]. Poverty to income variable is an index for the ratio of family income to poverty. The Department of Health and Human Services' (HHS) poverty guidelines were used as the poverty measure to calculate this index [20]. For the assessment of height and weight during the physical examination, participants were dressed in underwear, disposable paper gowns and foam slippers. A digital scale was used to measure weight to the nearest 100 g; a fixed stadiometer was used to measure height to the nearest mm. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m).

2.2. Independent variables

A blood specimen was drawn from an antecubital vein. Fasting blood glucose (FBG) was measured by a hexokinase method using a Roche/Hitachi 911 Analyzer. SUA was determined by the uricase-peroxidase technique [20]. Other laboratory-test details are available in the NHANES Laboratory/Medical Technologists Procedures Manual [20]. To obtain the participants' BP, the average of all available measures after a total of 4 attempted readings was used. BP was measured in the right arm unless otherwise specified. Smoking status was self-reported. The CKD Epidemiology Collaboration (CKD-EPI) equation was used to calculate the estimated glomerular filtration rate (eGFR, in ml/min/1.73 m^2) [21]. Levels of total serum cholesterol (TC) were measured enzymatically.

WBC was measured by Coulter HMX Haematology Analyzer, CRP levels were measured by latex enhanced nephelometry. For the calculation of the inflammatory score, Z-scores from biomarkers (CRP and WBC) were summed up. The AIP was calculated using the following formula: AIP = log(TG/HDL-C). Participants were assigned to 1 of 2 groups based on the AIP; those with an AIP < 0.21 were assigned to the low- or moderate-risk atherosclerosis group, whereas those with an AIP ≥ 0.21 were assigned to the high-risk atherosclerosis group [22]. CRP levels ≥ 3 mg/l was considered as an indicator of high CVD risk [23].

Details on recording dietary intake have been previously described [24,25]. Briefly, dietary intake was assessed via 24 h recall obtained by a trained interviewer, with the use of a computer-assisted dietary interview system with standardized probes, i.e. the United States Department of Agriculture Automated Multiple-Pass Method (AMPM) [24,25]. The AMPM is designed to enhance complete and accurate data collection while reducing respondent burden [25,26]. The United States Department of Agriculture (USDA) Food and Nutrient Database for Dietary Studies was used to determine the nutrient content of foods during the NHANES survey.

2.3. Cardiovascular health (CVH)

CVH was assessed based on 7 metrics: smoking status, physical activity, diet, BMI, total cholesterol, FBG and BP. Each metric was categorized into 3 levels of "poor," "intermediate" and "ideal" and assigned

scores of 0, 1, and 2, respectively, according to the AHA definitions (as outlined in Supplementary Table 1) [13]. A total CVH score was calculated by summing scores for each of the 7 CVH metrics, ranging from 0 to 14, with the highest score indicating a better CVH. Total CVH score was then categorized into poor (0–7), intermediate (8–10), or ideal (11–14) levels of CVH, according to the literature [13].

Smoking status was categorized as ideal (never smokers, those who reported never having smoked 100 cigarettes during their lifetime), intermediate (former smokers, those who reported smoking at least 100 cigarettes during their lifetime but currently did not smoke), and poor (current smokers, those who smoked 100 cigarettes during their lifetime and were still currently smoking).

Physical activity was assessed based on the frequency and duration of moderate and vigorous intensity of leisure, transportation, and household activities and classified as ideal (≥150 min/week moderate intensity, ≥75 min/week vigorous intensity or equivalent combination), intermediate (1–149 min/week moderate intensity, 1–74 min/week vigorous intensity or equivalent combination) and poor (no moderate and vigorous activity). BMI was classified as ideal (< 25 kg/m^2), intermediate (25 to < 30 kg/m^2) and poor (≥30 kg/m^2).

The healthy dietary score was assessed based on the Healthy Eating Index-2005 (HEI-2005). The HEI-2005 is a measure of diet quality that evaluates the extent to which an individual's dietary conforms to the 2005 US Dietary Guidelines [27]. It is composed of 12 nutrients- and food-based components collected by 24-h dietary recalls. The first 6 components, including total fruit, whole fruit, total vegetables, dark green and orange vegetables and legumes, and total grains and whole grains, are each given a score of 0–5 points. The next 5 components, including milk, meat and beans, oils, saturated fat (SFA), and sugar, are each given 0 to 10 points. The last component that reflects calories from solid fat, alcohol, and added sugars is given 0 to 20 points. The total HEI-2005 scores of the 12 components range from 0 to 100. In this analysis, participants with an HEI-2005 score < 50 were categorized as having poor diet quality, those with a score of > 50 to < 81 as intermediate diet quality and those with a score of ≥81 as ideal diet quality, as previously defined [28].

Total cholesterol status was classified as ideal (untreated and < 200 mg/dL), intermediate (treated to < 200 or 200–239 mg/dL) and poor (≥240 mg/dL). FBG was classified as ideal (untreated and < 100 mg/dL), intermediate (treated to < 100 or 100–125 mg/dL) and poor (≥126 mg/dL). BP was classified as ideal (untreated and < 120/< 80 mmHg), intermediate (treated to < 120/< 80 mmHg or 120–139/80-89 mmHg) and poor (≥140/90 mmHg).

2.4. Statistical analysis

Analyses were conducted using the SPSS software (version 22, Chicago, IL, USA) according to the guidelines set by the center for disease control (CDC) for analysis of complex NHANES datasets, accounting for the masked variance and using the proposed weighting methodology [29]. We used mean and standard error of mean (SEM) for continuous measures (analysis of variance) and percentages for categorical variables (Chi-square). Adjusted [for age (continuous), gender (dichotomized), race (categorical), poverty to income ratio (continuous), education (categorical) and marital status (categorical)] linear regression was performed to evaluate the associations of the CVH score with the inflammatory score, SUA and AIP. In linear regression, CVH score was used as the dependent factor, whereas the inflammatory score, SUA and AIP as independent variables in each model. Adjusted [for age (continuous), gender (dichotomized), race (categorical), poverty to income ratio (continuous), education (categorical) and marital status (categorical)] logistic regression was performed to determine the link between "high-risk atherosclerosis" and "CVD risk" with each CVH metric, including smoking, BMI, physical activity, diet score, TC, BP and FBG (poor considered as reference in logistic regression). The results of the linear regression were expressed as standardized beta-coefficients (β). In logistic regression, "high-risk atherosclerosis" (dichotomized, AIP ≥0.21 = 1 *vs.* AIP < 0.21 = 0) or "CVD risk" (dichotomized, CRP ≥3 = 1 *vs.* CR*P* < 3 = 0) were used as dependent factors, whereas the CVH metric (dichotomized) was used as an independent variable in each model. The results of the logistic regression were expressed as odds ratio (OR) and 95% confidence interval (95%CI).

Because of the importance of the effect of eGFR on circulating levels of SUA, we have corrected our model. In this regard because eGFR was already influenced by age, gender and race we took these three factors (age, gender and race) out of the model to decrease the chance of co-linearity when considering SUA values [21]. Multi-collinearity for the multiple linear regressions was assessed with variance inflation factors (VIF) at each step [30]. Multi-collinearity was considered high when the VIF was > 10 [30]. Furthermore, in the same model, we calculated "high-risk atherosclerosis" and "high CVD risk" across the categories of CVH (poor level of CVH (score 0–8) was considered as reference in models). A two-sided $p \leq 0.05$ was considered significant.

3. Results

We included 23,004 participants with a mean age of 47.2 years (males: 47.6 ± 0.1 *vs.* females: 46.8 ± 0.1, $p = 0.089$). Males compromised 46.5% of the total population. The characteristics of the population according to CVH categories are shown in Table 1. Participants with an ideal CVH level were significantly younger than those with intermediate and poor level ($p < 0.001$, Table 1). The majority of participants with poor and intermediate CVH level were male, whereas females were the majority in the ideal CVH category (59.1 *vs.* 41.0%, $p < 0.001$, Table 1). With regard to

Table 1
Characteristics of study participants according to CVH categories.

Characteristic		Total sample	Poor (score 0–8) (n = 7591)	Intermediate (score 9–10) (n = 10423)	Ideal (score 11–14) (n = 4990)	*p*
Age (year)		47.2 ± 0.2	48.9 ± 0.1	42.8 ± 0.3	38.2 ± 0.2	< 0.001
Gender	Men (%)	46.5	56.3	58.9	41.0	< 0.001
	Women (%)	53.5	43.7	41.1	59.1	
Race/Ethnicity	Non-Hispanic White (%)	48.2	32.9	44.2	22.9	< 0.001
	Non-Hispanic Black (%)	21.1	39.4	46.3	14.3	
	Mexican-American (%)	31.2	26.4	51.3	22.3	
Education	Less than high school (%)	29.4	46.3	42.1	11.6	< 0.001
	Completed high school (%)	21.1	38.5	41.2	20.3	
	More than high school (%)	34.5	25.3	44.1	30.6	
Poverty income ratio		2.8 ± 0.09	2.9 ± 0.08	3.2 ± 0.07	3.6 ± 0.07	< 0.001
C-reactive protein (mg/dl)		0.46 ± 0.02	0.51 ± 0.01	0.49 ± 0.01	0.38 ± 0.01	< 0.001
White blood cells (x10^9)		7.0 ± 0.02	7.1 ± 0.02	7.0 ± 0.03	7.0 ± 0.02	0.239
Serum uric acid (mg/dl)		5.1 ± 0.01	5.3 ± 0.01	5.2 ± 0.02	5.1 ± 0.01	< 0.001
Atherogenic index of plasma		0.92 ± 0.03	0.95 ± 0.02	0.94 ± 0.03	0.86 ± 0.01	< 0.001

CVH: cardiovascular health.
Values expressed as mean ± standard error of mean and %. Chi-square or analysis of variance was applied to compare the groups.

Table 2
Linear association between inflammatory score, SUA and AIP with each CVH score.

	inflammatory score		SUA		AIP	
	β	*p*-value	β	*p*-value	β	*p*-value
CVH score	−0.052	< 0.001	−0.041	< 0.001	−0.039	< 0.001

CVH: cardiovascular health, β: standardized beta-coefficient, SUA: serum uric acid, AIP: atherogenic index of plasma.
Model adjusted for age, gender, race, poverty to income ratio, education and marital status.

race/ethnicity, non-Hispanic White (22.9%) and non-Hispanic Black (39.4%) consisted the majority of participants with ideal and poor CVH ($p < 0.001$). Furthermore, participants with an ideal CVH level had the highest ratio of poverty to income (3.62%) followed by intermediate (3.20%) and poor CVH categories (2.92%, $p < 0.001$). Participants with a higher score of CVH (ideal CVH) had lower levels of CRP, SUA and AIP ($p < 0.001$ for all comparisons, Table 1).

In adjusted (for age, gender, race, poverty to income ratio, education and marital status) linear regression, significant negative associations were observed between CVH score (dependent factor) and inflammatory score (independent factor) ($\beta = -0.052$, $p < 0.001$), SUA (independent factor) ($\beta = -0.041$, $p < 0.001$) and AIP (independent factor) ($\beta = -0.039$, $p < 0.001$), i.e. participants with a better (greater) CVH score had a lower inflammatory score (Table 2).

We have calculated the adjusted (for age, gender, race, poverty to income ratio, education and marital status) association between the likelihood of "high-risk atherosclerosis, AIP ≥0.21" (dichotomized) and "high CVD risk, CRP ≥3 mg/l" (dichotomized) with each CVH metric (Table 3). We found that for both dependent variables ("high-risk atherosclerosis" and "CVD risk") and for each CVH component, participants with a higher score (ideal) had a lower likelihood for "high-risk atherosclerosis" and "CVD risk".

Adjusted (for age, gender, race, poverty to income ratio, education and marital status) logistic regression was performed to evaluate the odds of "high-risk atherosclerosis, AIP ≥0.21" (dichotomized) and "high CVD risk, CRP ≥3 mg/l" (dichotomized) across CVH categories. There was a reduction in the likelihood of "high-risk atherosclerosis" [intermediate = OR: 0.90, 95%CI: 0.85–0.95, ideal = OR: 0.81, 95%CI: 0.74–0.88] and "CVD risk "[intermediate = odds ratio (OR): 0.86, 95% confidence interval (CI):0.73–0.98, ideal = OR: 0.82, 95%CI: 0.69–0.95] across the categories of CVH.

4. Discussion

By using a large nationally representative sample of US adults, we evaluated the link between inflammatory score, SUA, AIP and CVH level proposed by the AHA. We found that participants with a higher CVH level (i.e. healthier) had a lower score of inflammation, SUA and AIP. Furthermore, there was an inverse link of CVH level with "high-risk atherosclerosis, AIP ≥0.21" and "high CVD risk, CRP ≥3 mg/l". These findings were robust after correction for a wide range of confounders.

A cross-sectional analysis between 543 adolescents (251 boys and 292 girls) from the HELENA study [15] reported that there is an association between the ideal CVH and inflammatory status in adolescence, which is in accordance with another study [15]. There is just a single cross-sectional study on the link between CRP and CVH score in a Chinese general population, reporting an inverse relationship between the number of ideal health metrics and CRP [16].

Previous studies reported an association of CVH components with CRP and inflammation, for example, in a population-based study of a healthy middle-aged male population, CRP levels were significantly reduced with increasing intensity physical activity (median CRP was 1.81 mg/l in the population with no physical activity in comparison to 1.28 mg/L in those who performed moderate physical activity and 0.88 mg/L in those with vigorous physical activity) [31]. Similarly, Ford et al. observed that the OR of increased CRP levels (≥4.4 mg/L in males and ≥7.0 mg/L in females) in the groups with light, moderate, and vigorous intensity physical activity were 0.98 (95%CI: 0.78–1.23), 0.85 (95%CI: 0.70–1.02) and 0.53 (95%CI: 0.40–0.71), respectively, compared with a group with no physical activity, suggesting that physical activity plays an important anti-inflammatory role [32].

Diet is another ideal CVH behaviour associated with chronic inflammation [33–37]. We have previously reported a direct link between SFA and *trans* fatty acid (TFA) with CRP, as well as a reverse association between polyunsaturated fatty acids (PUFA) and CRP [35,36]. Participants with a higher intake of mineral and vitamins (diet rich in fruits and vegetables) had a lower level of inflammatory factors [35,36]. In this context, we demonstrated a reverse link between minerals and vitamins intake with the risk of peripheral artery disease [38], as well

Table 3
Association between likelihood of "high-risk of atherosclerosis" and "high CVD risk" with each CVH components.

CVH variable and class		High-risk atherosclerosis		High CVD risk	
		Prevalence Ratio	95% confidence interval	Prevalence Ratio	95% confidence interval
Smoking	Ideal	0.84	0.72–0.96	0.82	0.77–0.87
	Intermediate	0.91	0.83–0.99	0.86	0.74–0.97
Body mass index	Ideal	0.82	0.77–0.93	0.76	0.70–0.82
	Intermediate	0.86	0.79–0.93	0.91	0.88–0.94
Physical activity	Ideal	0.79	0.71–0.87	0.94	0.90–0.97
	Intermediate	0.84	0.75–0.93	0.92	0.87–0.96
Diet score	Ideal	0.88	0.79–0.96	0.77	0.71–0.83
	Intermediate	0.92	0.90–0.94	0.82	0.77–0.87
Total cholesterol	Ideal	0.87	0.80–0.94	0.87	0.80–0.94
	Intermediate	0.93	0.90–0.97	0.92	0.90–0.94
Blood pressure	Ideal	0.83	0.77–0.89	0.88	0.81–0.95
	Intermediate	0.90	0.86–0.94	0.93	0.90–0.96
Fasting plasma glucose	Ideal	0.79	0.71–0.87	0.84	0.80–0.89
	Intermediate	0.95	0.93–0.97	0.89	0.82–0.96

Poor level of CVH (score 0–8) was considered as reference in the models. Adjusted logistic regression was applied.
AIP: atherogenic index of plasma, CRP: C-reactive protein, CVD: cardiovascular disease, CVH: cardiovascular health.
Model adjusted for age, gender, race, poverty to income ratio, education and marital status.
Definitions:high-risk atherosclerosis = AIP ≥0.21.
High CVD risk = CRP ≥3 mg/l

as a direct association of plasma TFAs levels with an unfavourable profile of inflammatory and cardiometabolic factors [39,40]. Another study demonstrated that high vegetable and fruit consumption may improve endothelial function, alleviate insulin resistance, reduce body weight, lower BP, and beneficially affect lipid metabolism [41]. We have also reported that diet heavily loaded with carbohydrate, SFA and total fat foods was associated with impaired glucose tolerance; in contrast, a diet rich in vitamins, minerals and fibres, had favourable effects on insulin sensitivity and glucose tolerance [34]. We have previously reported that, individuals with higher CRP levels had a greater risk of MetS and hypertension [42] which are CVD risk factors; a direct association was also observed between CRP levels and the number of MetS components, i.e. the higher the CRP level, the greater the number of MetS components [42].

With regard to SUA, in the present study, participants with a higher CVH score (i.e. more favourable) had lower SUA levels. In previous studies, SUA was considered a risk predictor for CVD and other non-communicable diseases such as T2D; for example, in a population-based and cohort study (10,000 men) SUA levels were higher in pre-diabetic than in non-diabetic participants [43]. Furthermore, SUA levels were linked to the incidence of impaired fasting glucose and T2D, suggesting that hyperuricaemia is a predictor for the development of insulin resistance, pre-diabetes and T2D [44,45]. Apart from a direct effect of SUA, it has been suggested that SUA may be related to inflammation and CVD via induction of CRP mRNA expression in human vascular endothelial and smooth muscle cells [46]. A significant positive correlation between CRP, TNF-α and IL-6 with SUA was also suggested [47,48]. Recently, we reported that participants with higher SUA levels had a less favourable profile of glucose/insulin homeostasis parameters [49]. However, because of controversial epidemiological findings and the lack of consistent evidence, whether SUA is an independent and causal risk factor for CHD, stroke and cancer still remains unknown [50–54]. Several observational studies [5,50,54,55] demonstrated that elevated SUA might predict CHD risk. However, other studies contradicted this evidence [51,56–59]. Several meta-analyses of observational studies found that hyperuricaemia could significantly increase the risk of CHD events [59–61]. These studies were restricted by heterogeneity of the sample. Furthermore, previous meta-analyses did not assess important differences between studies (e.g. sample size, other characteristics that may contribute to these inconsistencies such as geographical location, baseline SUA levels, gender and obesity, as well as study quality and duration of follow-up). The result from 417,734 participants supported a positive association between hyperuricaemia and risk of CHD both in males and in females [62]. Of note, eGFR is also an important factor, which has been ignored in many of studies. In the current study, because of the model limitation, we were also not able to investigate this, but we strongly advise to take account of this variable in future studies for the link between SUA and cardio-metabolic risk factors [5,63].

We also evaluated the link between the CVH score and AIP. This relationship has been evaluated in two Chinese studies [17,18]. Shen et al. (n = 27,824 middle-aged Chinese men) and Chang et al. (n = 11,113 middle-aged Chinese people) reported a reverse link between the CVH score and AIP, i.e. subjects with a higher CVH score had a lower AIP score [17,18]. Furthermore, Chang et al. found that all of the 7 CVH metrics significantly correlated with AIP, which is in line with our results [18]. However, the Chen et al. study had some limitations; for example, participants were from rural areas of China. Furthermore, some criteria for ideal CVH were adjusted for BMI, physical activity and diet score, which may hamper comparisons with other studies [18]. Epidemiological data showed associations of BMI, FPG, total cholesterol, diet, BP, physical activity, and smoking with AIP [17,64–66], which is in accordance with our results, as an inverse relationship existed between the number of ideal CVH metrics and the prevalence of a high AIP.

Our findings may have public health implications as they show that participants with inadequate CVH are at a high risk for atherosclerosis and CVD. However, these findings should be interpreted with caution because of the study design. Therefore, health education and lifestyle interventions tailored to these high-risk populations should be considered to improve CVH behaviours and factors. The AHA's 2020 Strategic Impact Goals was introduced to reduce the burden of CVD and stroke morbidity and mortality by achieving an ideal CVH [13]. The concept of ideal CVH behaviours and factors, and their value in predicting high risk of developing CVD, should be implemented in populations to promote health status among high risk populations with poor CVH. In this context, the 7 CVH metrics should be improved among middle-aged populations with overweight/obesity, smoking, poor diet score, and physical inactivity. In addition, BP, FPG, and blood lipids should be monitored periodically and medications should be timely adjusted in order to achieve and maintain normal values.

The main limitation of our study is that the associations between CVH and independent variables were only evaluated at 1 point in time. This was a cross-sectional study and could not definitively provide causal relationship between the health factors/behaviours and the prevalence of high AIP. Although we have adjusted for important potential confounders and mediators, residual confounders correlating with both CVH and independent variables may still exist, including other chronic diseases (e.g. cancer), menopausal status, sex-hormones, medication use, and genetic, behavioural, psychosocial and environmental factors. Furthermore, physical activity and diet were evaluated based on self-reports, so misclassification attributed to recall bias and measurement errors may underestimate some of the observed associations.

Despite these limitations, our study is unique as, to the best of our knowledge, we are the first to report the association between SUA and CVH as defined by the AHA. The present study was conducted in a large, ethnically diverse, and representative sample of US adults, suggesting that our findings might be generalizable. Finally, the use of reliable and standardized measures of CVH and independent variables are also of large importance.

In conclusion, our findings suggest that, in a nationally representative population of US adults, CVH metrics were associated with inflammatory score, SUA and AIP. These results reinforce the importance of healthy behaviours as proposed by the AHA. If confirmed in clinical trials, this knowledge may have implications for the prevention and management of CVD.

Conflicts of interest

NK has given talks, attended conferences and participated in trials sponsored by Amgen, Angelini, Astra Zeneca, Boehringer Ingelheim, MSD, Novartis, NovoNordisk, Sanofi and WinMedica. DPM has given talks and attended conferences sponsored by MSD, AstraZeneca and Libytec. The other authors have no conflict of interest to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.atherosclerosis.2018.09.016.

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