Association Between Weight Change and Increased Likelihood of Abdominal Aortic Calcification Among Men

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Abstract
Objective: We aimed to explore the effect of weight change on abdominal aortic calcification (AAC) among men.

Methods: Data were obtained from the 2013 to 2014 National Health and Nutrition Examination Survey (NHANES). Self-reported cardiovascular disease patients were excluded. Lateral spine images were used to quantify AAC score and severe AAC was defined as a AAC score greater than 6. Weight change over a 10-year period was defined as long-term weight change, and weight change over a 1-year period was defined as short-term weight change. The relationship between long-term and short-term weight change with AAC grade was estimated by using multivariable regression analysis and subgroup analysis.

Results: After adjusting for covariates, weight gain, especially severe weight gain (> 10 kg), was associated with increased likelihood of AAC and severe AAC both in the short term (1 year) and long term (10 years) among men when compared to stable weight change, while long-term weight loss could also lead to an increased likelihood of AAC and severe AAC.

Conclusion: Stable body weight might be a predictor of a lower risk of AAC and severe AAC among men in the long term and short term.

Key Words: weight change, abdominal aortic calcification, vascular calcification, males, NHANES, cross-sectional study

Abbreviations: AAC, abdominal aortic calcification; BMI, body mass index; CAC, coronary artery calcification; CVD, cardiovascular disease; NHANES, National Health and Nutrition Examination Survey; IMT, intima-media thickness; MONW, metabolically obese, normal-weight; PIR, income to poverty ratio.

Accumulating evidence has demonstrated that obesity and weight gain are independent risk factors for hypertension [1], dyslipidemia [2], and cardiovascular disease (CVD) [3, 4], thus intentional weight loss is recommended to overweight and obese patients based on such settings. However, the obesity paradox has been observed in several population-based samples in which overweight and obese patients had lower odds of in-hospital mortality [5] and better prognosis [6] compared to normal-weight patients. Even so, weight loss as a primary treatment strategy for AAC with regard to weight management among males, we carried out a study to explore the possible correlation between both.

Vascular calcification is a clinical marker of atherosclerosis [13], which can result in CVDs [14] and lead to a poorer prognosis, comprising higher mortality risk, adverse cardiovascular events, and other comorbidities. The presence of calcified plaque in the aorta [15] is considered as a well-characterized marker of vascular calcification and a predictor both of cardiovascular and all-cause mortality [16]. The abdominal aortic calcification (AAC) grading quantification method (AAC score) was created to evaluate the severity of calcified vessels by using lateral lumbar radiography, which was thought could reflect aortic calcification, grade lumbar aortic calcification, and create composite summary scores that are reproducible [17, 18]. To the best of our knowledge, no previous study has explored the relationship between long- and short-term weight change with AAC [19] score and severe AAC. To establish an appropriate preventive strategy for AAC with regard to weight management among males, we carried out a study to explore the possible correlation between both.

Materials and Methods

Study Population

Data were obtained from the 2013 to 2014 National Health and Nutrition Examination Survey (NHANES), the design of which has been described in detail before [20]. Male participants with a full set of data both on AAC score and weight change were included. Patients with self-reported CVD were excluded, which including angina, coronary heart disease,
congestive heart failure, heart attack, or stroke. Ultimately we included 1249 men in the main analyses.

**Survey and Measurement**

Demographic information was collected using a standard questionnaire, including age, race (Mexican American, non-Hispanic White, non-Hispanic Black, and other), educational level (< high school, high school or equivalent, and ≥ college), and income to poverty ratio (PIR) [21]. The lifestyle of participants was characterized by energy intake, physical activity, alcohol consumption (drinker, nondrinker), and smoking status (never, former, current smoker). Participants who performed at least 2.5 hours of moderate-intensity activity, 1.25 hours of vigorous-intensity activity, or an equal combination of moderate- and vigorous-intensity activity per week were defined as physically active. A participant who consumed at least 12 alcoholic beverage in any 1 year was defined as a drinker. The medical comorbidities included self-reported diabetes (yes, no) and hypertension (yes, no). The height and weight of the participants were recorded by professionals. Participants were required to recall their weight at 1 and 10 years before the survey. By dividing absolute weight change into 5 groups, we derived a new patterns of weight change: less than –2.5 kg (weight loss), –2.5 to 2.5 kg (stable weight, reference group), 2.5 to 5.0 kg (mild weight gain), 5.0 to 10.0 kg (moderate weight gain), and greater than or equal to 10.0 kg (severe weight gain). The AAC grading quantification method (AAC score) was established to assess the severity of calcified vessels by using lateral lumbar radiography, and severe AAC was defined as an AAC score greater than 6.

**Statistical Analysis**

General characteristics are described as median (interquartile range) based on data distribution; categorical variables are presented as proportions. According to severe AAC status, differences in general characteristics were compared using the Wilcoxon rank sum test for continuous variables and chi-square for categorical variables. We explored the relationship between 5 weight change patterns at each time point and AAC scores and severe AAC. Stable weight change was chosen as the reference level. We used multivariate regression models and subgroup analysis to analyze the relationship between long- or short-term weight change and the grade of AAC. Model 1 was the unadjusted model. Model 2 included age and race. Model 3 further included body mass index (BMI) at 1 or 10 years prior, energy intake, physical activity, alcohol use, smoking status, diabetes, and hypertension, along with the covariates in model 2. All analyses were conducted using the tableone and foreign package from R software v4.1.2 and Free Statistics software (version 1.1). A 2-tailed test was conducted and a P value less than .05 was considered statistically significant.

**Results**

A total of 1249 men without known CVD from the NHANES 2013 to 2014 cycles were enrolled in the study (Fig. 1).

The study population characteristics are shown in Table 1. Compared with the reference group, the participants with severe AAC (AAC score > 6) were older and had a higher smoking rate and a higher prevalence of diabetes and hypertension. Lower weight, regardless of current weight or weight change, was associated with a higher risk of severe AAC. The results of the subgroup analysis are shown in Table 2. The associations were stronger in older and lower BMI participants. The results of the multivariate regression analysis are shown in Table 3. The associations were stronger in the models that included BMI and other covariates.
1 or 10 years prior, was observed among severe AAC patients, and long-term weight loss was associated with severe AAC. In addition, there were statistically no significant associations between severe AAC and race, education level, PIR, energy intake, alcohol use, and short-term weight change.

We first explored the relationship between AAC score with 5 weight change patterns at each time point. None was adjusted in model 1. Model 2 included age and race. Model 3 further included BMI at 1 or 10 years prior, energy intake, physical activity, alcohol use, smoking status, diabetes, and hypertension, along with the covariates in model 2 (Table 2). After adjusting for covariates, we found that compared with the stable weight change, severe weight gain (>10 kg) within 1 year was associated with an increased likelihood of AAC (β = 2.18; 95% CI, 0.91-3.45), while short-term weight loss was associated with elevated AAC score (β = 0.73; 95% CI, 0.16-1.3). When it comes to weight change within 10 years, any weight gain was associated with increased AAC score, and a statistically significant correlation was found between weight loss and increased AAC score (β = 0.62; 95% CI, 0.04-1.2) (see Fig. 2).

We further explored the relationship between weight change at each time point and severe AAC. In the short-term, severe weight gain (>10 kg) was statistically significantly associated with severe AAC (odds ratio = 18.97; 95% CI, 3.37-106.74) when compared with stable weight change. The same positive association was observed between long-term weight change and severe AAC (odds ratio = 4.81; 95% CI, 1.02-22.73), whereas severe AAC was associated with long-term weight loss only (odds ratio = 3.59; 95% CI, 1.2-10.75), not with short-term weight loss (Fig. 3).

### Discussion

Our study found that compared with stable weight change, weight gain, especially severe weight gain, was associated with increased likelihood of AAC and severe AAC both in short-term
and in long-term life among men, whereas long-term weight loss could also lead to the increased likelihood of AAC and severe AAC. Our finding suggests that stable body weight, no matter in the long term or short term, might be a predictor of a lower risk of AAC and severe AAC among men.

To our knowledge, the association between weight change and the development of vascular calcification is not well studied; current studies in this field have mainly focused on coronary artery calcification (CAC) and related-cardiovascular events, and have not addressed AAC. The presence of calcified plaque in the coronaries [22, 23] and also the aorta [15] is considered a reliable marker of atherosclerosis [24]. Among several vascular calcification scores [25, 26] on plain radiograph, the AAC score is the most reliable predictor of severe CAC, and can be used to predict CVD [27, 28]. Studies have revealed that severe CAC is related to weight loss, modest weight gain, and weight fluctuation [29]. BMI change during adolescence is an independent predictor of CAC score and risk of acute coronary events in adult men [30]. In several observational studies, investigators have reported that both weight gain and loss carried an excess risk for all-cause and CVD mortality in middle-aged and older individuals [31]; a similar result was found in adults with insulin-treated diabetes [32] in a predialysis, chronic kidney disease population.

Table 2. Multivariate linear regression analysis of weight change and abdominal aortic calcification score at each time point

| Subgroup | Model 1 | Model 2 | Model 3 |
|----------|---------|---------|---------|
|          | OR (95% CI) P | OR (95% CI) P | OR (95% CI) P |
| Short term, 1 y | | | |
| Weight change within 2.5 kg | 0 (Reference) | 0 (Reference) | 0 (Reference) |
| Weight lost > 2.5 kg | 0.19 (-0.21–0.6) .344 | 0.26 (-0.12–0.64) .182 | 0.73 (0.16–1.3) .012 |
| 2.5 kg < weight gain < 5 kg | -0.48 (-1.07–0.1) .106 | -0.03 (-0.58–0.53) .927 | 0.14 (-0.67–0.95) .736 |
| 5 kg < weight gain < 10 kg | -0.67 (-1.42–0.09) .086 | -0.24 (-0.96–0.48) .51 | -0.05 (-1.09–0.98) .92 |
| Weight gain > 10 kg | 0.43 (-0.5–1.35) .366 | 0.86 (-0.01–1.73) .053 | 2.18 (0.91–3.45) .001 |
| Long term, 10 y | | | |
| Weight change within 2.5 kg | 0 (Reference) | 0 (Reference) | 0 (Reference) |
| Weight lost > 2.5 kg | 0.44 (0.01–0.87) .044 | 0.49 (0.09–0.9) .017 | 0.62 (0.04–1.2) .036 |
| 2.5 kg < weight gain < 5 kg | 0.28 (-0.25–0.81) .306 | 0.51 (0.01–1.01) .044 | 0.69 (0.02–1.37) .045 |
| 5 kg < weight gain < 10 kg | -0.22 (-0.72–0.27) .376 | 0.32 (-0.15–0.79) .183 | 0.71 (0.05–1.36) .035 |
| Weight gain > 10 kg | -0.39 (-0.88–0.09) .11 | 0.24 (-0.23–0.7) .318 | 0.92 (0.21–1.64) .012 |

None was adjusted in model 1; model 2 included age and race; model 3 further included body mass index at 1 or 10 years prior, energy intake, physical activity, alcohol use, smoking status, diabetes, and hypertension, along with covariates in model 2.

Abbreviation: OR, odds ratio.

Figure 2. Associations of abdominal aortic calcification score with 5 weight change patterns at each time point. Adjusted for age, race, body mass index at 1 or 10 years prior, energy intake, physical activity, alcohol use, smoking status, diabetes, and hypertension.
In addition, body-weight fluctuation was associated with an increased risk for venous thromboembolism [34], stroke [35], and cardiovascular events [36]. Other subclinical markers of atherosclerosis, like carotid artery intima-media thickness (IMT), were found to be associated with weight gain in numerous studies [37, 38], whereas there were contradicting results between weight loss and change in IMT [39-44]. However, varying associations with weight dynamics depending on which marker was used can explained this inconsistency between IMT and CAC [29]. All of these seem to suggest that weight fluctuation appear to increase CAC and CVD risk. Our finding was consistent with previous studies; however, it remains to be researched in clinical trials whether maintaining a stable body weight should be recommended to reduce the risk of vascular calcification.

The potential mechanisms behind the association between weight change and the grade of AAC are not known. In people with weight gain, excess adipose tissue and fat tissue dysfunction can result in dysregulated secretion of adipocytokines [45], which leads to osteogenic differentiation of vascular smooth muscle cells, vascular inflammation, and abnormal deposition of calcium and phosphorus in the vessel wall [46]. In addition, obesity is related to alterations in free fatty acid metabolism and deposition of ectopic fat [47, 48], such as perivascular adipose tissue, which can lead to the pathogenesis of calcified atherosclerosis via paracrine pathways [49]. Moreover, obesity has been associated with other CVD risk factors such as dyslipidemia, insulin resistance [50, 51], endothelial dysfunction [52, 53], and systemic oxidative stress, all of which are involved in the pathogenesis of calcified atherosclerosis [54]. As for individuals with weight loss, increased AAC likelihood may be due to sarcopenia. Studies have found that significantly more lean mass was lost with weight loss than was gained with weight gain, especially in older men [55, 56]. Of note, muscle wasting and sarcopenia were previously associated with increased risks of metabolic disorders, cardiovascular risk factors, physical disability, and mortality [57]. Another explanation may concern the presence of a “metabolically obese, normal-weight (MONW)” population, which is defined as lean individuals with multiple cardiometabolic risk factors. Members of the MONW population typically have the following characteristics: excessive visceral adipose tissue and ectopic fat deposits, adipose tissue inflammation, altered inflammation and adipokine profiles, decreased skeletal muscle mass, and low cardiorespiratory fitness [58], all of which may lead to vascular calcification.

However, several shortcomings need to be interpreted. First, the work presented here uses recalled weight from the remote past, although studies have shown that a bias in recall of past weight is smaller than that seen in recall of current weight [59, 60]. Second, there is a lack of baseline data on AAC. For analyses of individuals 10 years ago, participants may have already had AAC before the weight change interval; thus, we cannot rule out the presence of some reverse causality. Third, weight includes fat mass, lean body mass, and muscle mass, thus which body component changes affected the association with CVD risk could not be evaluated. Fourth, weight change does not distinguish the change of body fat distribution. Measuring fat distribution can help identify individuals at higher risk. Increased visceral fat can predict the development of AAC and other CVD risks better than total body fat alone.

In summary, this study suggests that stable body weight, no matter in the long term or short term, might be a predictor of a lower risk of AAC and severe AAC among men. Further studies with weight management intervention and a prospective study design are warranted to replicate our observations.

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Disclosures
The authors have nothing to disclose.
Data Availability

Original data generated and analyzed during this study are included in this published article or in the data repositories listed in “References.”

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