*Journal of the Endocrine Society*, 2022, **6**, 1–7
https://doi.org/10.1210/jendso/bvac067
Advance access publication 22 April 2022
**Research Article**

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

**Yanting Huang,[1] Zhijie Ruan,[1] Weizhao Lin,[1,2] Zhichao Chen,[1,2] Liling Zhang,[1,3] and Zhi Li[1,2]**

[1]Shantou University Medical College, Shantou, Guangdong 515041, P. R. China
[2]Department of Cardiology, the Second Affiliated Hospital of Shantou University Medical College, Shantou, Guangdong, P. R. China; and
[3]Endocrinology Department, the Second Affiliated Hospital of Shantou University Medical College, Shantou, Guangdong, P. R. China

**Correspondence:** Zhi Li, Department of Cardiology, the Second Affiliated Hospital of Shantou University Medical College, No. 69, Dongxiabei Rd, Shantou, Guangdong 515041, P. R. China. Email: lizhi519@126.com.

## 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 is recommended by the guidelines [7, 8]. Some studies showed a positive association between weight loss and CVD outcomes [9, 10], whereas higher CVD mortality was observed among patients with weight loss compared with overweight and moderately obese adults in several population-based samples [11, 12], all of which suggests a more varied pattern of association between the presence of overweight and obesity and weight change with mortality and CVD.

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,

**Received:** 10 February 2022. **Editorial Decision:** 20 April 2022. **Corrected and Typeset:** 4 May 2022

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

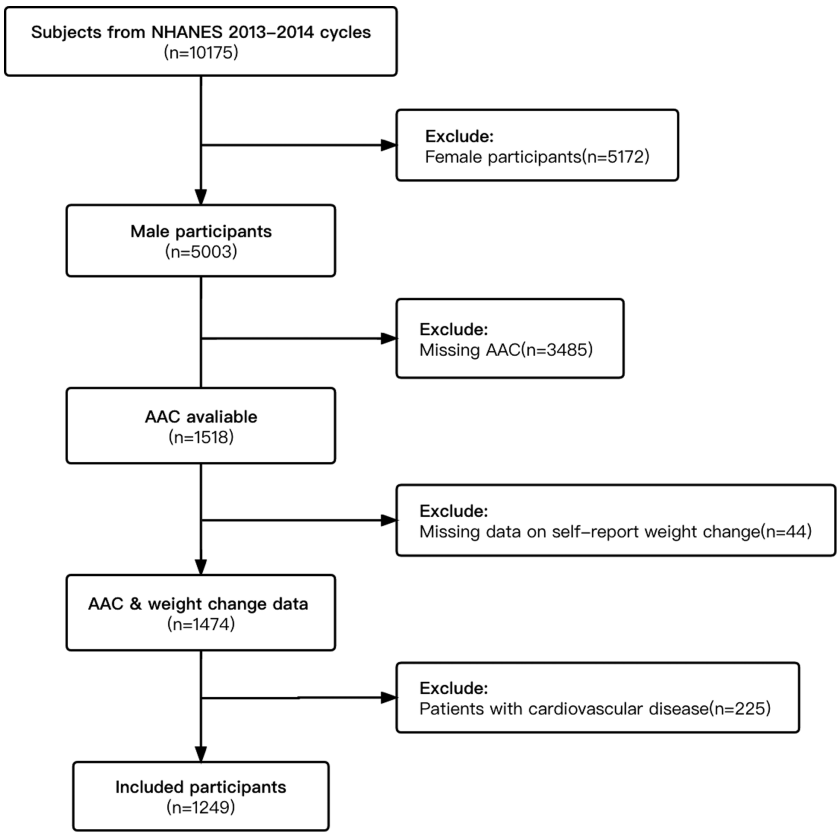


**Figure 1.** Flowchart of participant selection.

**Table 1.** Characteristics of the study population

| Characteristics | Overall | Nonsevere AAC | Severe AAC | *P* |
|---|---|---|---|---|
| No. | 1249 | 1170 | 79 | |
| Age, y | 56 (47 to 65) | 55 (47 to 64) | 71 (64 to 79) | < .01 |
| Race, % | | | | .02 |
| Mexican American | 290 (23.2) | 280 (23.9) | 10 (12.7) | |
| Non-Hispanic White | 511 (40.9) | 467 (39.9) | 44 (55.7) | |
| Non-Hispanic Black | 266 (21.3) | 253 (21.6) | 13 (16.5) | |
| Other | 182 (14.6) | 170 (14.5) | 12 (15.2) | |
| Education, % | | | | .69 |
| < High school | 286 (22.9%) | 266 (22.7%) | 20 (25.3%) | |
| High school or equivalent | 277 (22.2%) | 258 (22.1%) | 19 (24.1%) | |
| ≥ College | 686 (54.9%) | 646 (55.2%) | 40 (50.6%) | |
| Poverty income ratio | 2.73 (1.27 to 4.91) | 2.79 (1.27 to 4.97) | 2.28 (1.42 to 4.28) | .73 |
| Physical activity, % | | | | .09 |
| Inactive | 608 (64.7%) | 563 (64.1%) | 45 (75.0%) | |
| Active | 331 (35.3%) | 316 (35.9%) | 15 (35.0%) | |
| Energy, kCal/d | 2195 (1657 to 2851) | 2238 (1674 to 2862) | 1849 (1552 to 2431) | < .01 |
| Smoking status, % | | | | |
| Never | 572 (45.8) | 549 (47.0) | 23 (29.1) | < .01 |
| Past | 422 (33.8) | 386 (33.0) | 36 (45.6) | |
| Current | 254 (20.4) | 234 (20.0) | 20 (25.3) | |
| Alcohol use, % | | | | ≥ .999 |
| No | 827 (99.5%) | 775 (99.5%) | 52 (100.0%) | |
| Yes | 4 (0.5%) | 4 (0.5%) | 0 (0.0%) | |
| Diabetes, % | | | | <0.01 |
| No | 1015 (84.7%) | 963 (85.6%) | 52 (71.2%) | |
| Yes | 183 (15.3%) | 162 (14.4%) | 21 (28.8%) | |
| Hypertension, % | | | | < .01 |
| No | 754 (60.4%) | 726 (62.1%) | 28 (35.4%) | |
| Yes | 494 (39.6%) | 443 (37.9%) | 51 (64.6%) | |
| Short-term weight change | 0 (–1.81 to 0.91) | 0 (–1.81 to 0.91) | 0 (–2.27 to 0.45) | .92 |
| Long-term weight change | 2.27 (–2.27 to 6.80) | 2.27 (–2.27 to 6.80) | 0 (–6.80 to 4.54) | < .01 |
| Current weight | 83.5 (74.2 to 95.3) | 83.9 (74.8 to 95.3) | 75.7 (68.0 to 86.6) | < .01 |
| Weight at 1 y prior | 83.5 (74.4 to 95.3) | 83.9 (74.8 to 96.2) | 77.1 (68.0 to 85.3) | < .01 |
| Weight at 10 y prior | 80.7 (72.6 to 90.7) | 81.7 (72.6 to 90.7) | 76.2 (68.0 to 86.2) | .025 |

Abbreviation: AAC, abdominal aortic calcification.

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

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

| Subgroup | Model 1 | Model 2 | Model3 |
|---|---|---|---|
| | 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.

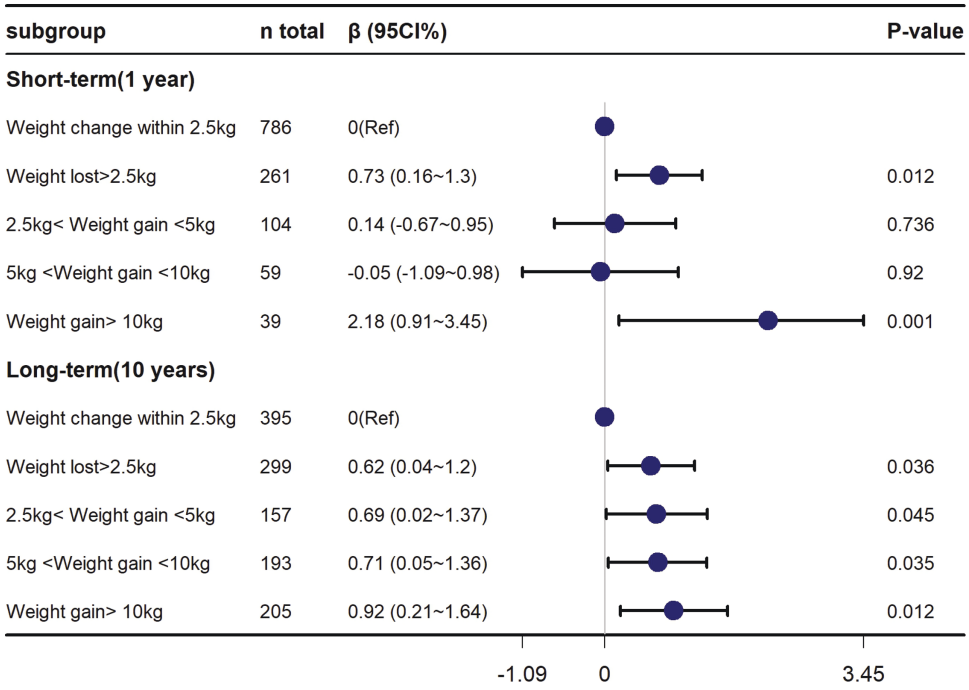


**Figure 2.** Associations of abdominal aortic calcification score with 5 weight change patterns at each time point. Adjusted for age, race, body mass index at 1 or 10 years prior, energy intake, physical activity, alcohol use, smoking statues, diabetes, and hypertension.

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

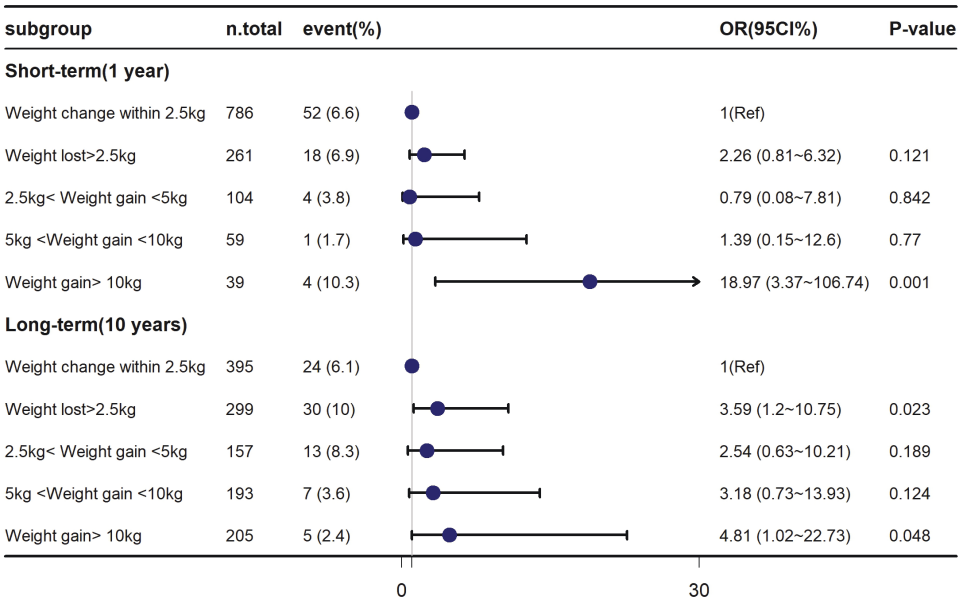


**Figure 3.** Associations of severe abdominal aortic calcification score with 5 weight change patterns at each time point. Adjusted for age, race, body mass index at 1 or 10 years prior, energy intake, physical activity, alcohol use, smoking statues, diabetes, and hypertension.

[33]. 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.

## Financial Support

This work was supported by the Guangdong Basic and Applied Basic Research Foundation (No. 2022A1515012454) of China.

## 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."

## References


1. Hall JE, do Carmo JM, da Silva AA, Wang Z, Hall ME. Obesity-induced hypertension: interaction of neurohumoral and renal mechanisms. *Circ Res*. 2015;116(6):991-1006.
2. Kim YJ, Lee YH, Lee YJ, Kim KJ, Kim SG. Weight gain predicts metabolic syndrome among North Korean refugees in South Korea. *Int J Environ Res Public Health*. 2021;18(16):8479.
3. Zhu Y, Zheng R, Hu C, *et al*. Association of early adulthood weight and subsequent weight change with cardiovascular diseases: findings from REACTION study. *Int J Cardiol*. 2021;332:209-215.
4. Honda T, Ishida Y, Oda M, *et al*. Changes in body weight and concurrent changes in cardiovascular risk profiles in community residents in Japan: the Hisayama Study. *J Atheroscler Thromb*. 2022;29(2):252-267.
5. Dhoot J, Tariq S, Erande A, Amin A, Patel P, Malik S. Effect of morbid obesity on in-hospital mortality and coronary revascularization outcomes after acute myocardial infarction in the United States. *Am J Cardiol*. 2013;111(8):1104-1110.
6. Timóteo AT, Ramos R, Toste A, Oliveira JA, Ferreira ML, Cruz Ferreira R. Impact of body mass index in the results after primary angioplasty in patients with ST segment elevation acute myocardial infarction. *Acute Card Care*. 2011;13(3):123-128.
7. Wadden TA, Tronieri JS, Butryn ML. Lifestyle modification approaches for the treatment of obesity in adults. *Am Psychol*. 2020;75(2):235-251.
8. Kushner RF, Ryan DH. Assessment and lifestyle management of patients with obesity: clinical recommendations from systematic reviews. *JAMA*. 2014;312(9):943-952.
9. Hasegawa Y, Nakagami T, Oya J, *et al*. Body weight reduction of 5% improved blood pressure and lipid profiles in obese men and blood glucose in obese women: a four-year follow-up observational study. *Metab Syndr Relat Disord*. 2019;17(5):250-258.
10. Strelitz J, Ahern AL, Long GH, *et al*. Moderate weight change following diabetes diagnosis and 10 year incidence of cardiovascular disease and mortality. *Diabetologia*. 2019;62(8):1391-1402.
11. Arafa A, Kokubo Y, Sheerah HA, *et al*. Weight change since age 20 and the risk of cardiovascular disease mortality: a prospective cohort study. *J Atheroscler Thromb*. Published online November 21, 2021. doi:10.5551/jat.63191
12. Ellis SG, Elliott J, Horrigan M, Raymond RE, Howell G. Low-normal or excessive body mass index: newly identified and powerful risk factors for death and other complications with percutaneous coronary intervention. *Am J Cardiol*. 1996;78(6):642-646.
13. Shi X, Gao J, Lv Q, *et al*. Calcification in atherosclerotic plaque vulnerability: friend or foe? *Front Physiol*. 2020;11:56.
14. Spence LA, Weaver CM. Calcium intake, vascular calcification, and vascular disease. *Nutr Rev*. 2013;71(1):15-22.
15. Wong ND, Lopez VA, Allison M, *et al*. Abdominal aortic calcium and multi-site atherosclerosis: the Multiethnic Study of Atherosclerosis. *Atherosclerosis*. 2011;214(2):436-441.
16. Martino F, Di Loreto P, Giacomini D, *et al*. Abdominal aortic calcification is an independent predictor of cardiovascular events in peritoneal dialysis patients. *Ther Apher Dial*. 2013;17(4):448-453.
17. Kauppila LI, Polak JF, Cupples LA, Hannan MT, Kiel DP, Wilson PW. New indices to classify location, severity and progression of calcific lesions in the abdominal aorta: a 25-year follow-up study. *Atherosclerosis*. 1997;132(2):245-250.
18. Bazzocchi A, Ciccarese F, Diano D, *et al*. Dual-energy x-ray absorptiometry in the evaluation of abdominal aortic calcifications. *J Clin Densitom*. 2012;15(2):198-204.
19. Mathiasen AB, Qayyum AA, Jørgensen E, *et al*. Bone marrow-derived mesenchymal stromal cell treatment in patients with severe ischaemic heart failure: a randomized placebo-controlled trial (MSC-HF trial). *Eur Heart J*. 2015;36(27):1744-1753.
20. Centers for Disease Control and Prevention. National Center for Health Statistics. NHANES 2013-2014, National Health and Nutrition Examination Survey. http://www.cdc.gov/nchs/nhanes.htm
21. Tellechea ML, Pirola CJ. The impact of hypertension on leukocyte telomere length: a systematic review and meta-analysis of human studies. *J Hum Hypertens*. 2017;31(2):99-105.
22. Vancheri F, Longo G, Vancheri S, Danial JSH, Henein MY. Coronary artery microcalcification: imaging and clinical implications. *Diagnostics (Basel)*. 2019;9(4):125.
23. Demer LL, Tintut Y. Vascular calcification: pathobiology of a multifaceted disease. *Circulation*. 2008;117(22):2938-2948.
24. Tsao CW, Pencina KM, Massaro JM, *et al*. Cross-sectional relations of arterial stiffness, pressure pulsatility, wave reflection, and arterial calcification. *Arterioscler Thromb Vasc Biol*. 2014;34(11):2495-2500.
25. Hong D, Ruan Y, Pu L, *et al*. Both pelvic radiography and lateral abdominal radiography correlate well with coronary artery calcification measured by computed tomography in hemodialysis patients: a cross-sectional study. *Hemodial Int*. 2016;20(3):399-406.
26. Takasu J, Budoff MJ, O'Brien KD, *et al*. Relationship between coronary artery and descending thoracic aortic calcification as detected by computed tomography: the Multi-Ethnic Study of Atherosclerosis. *Atherosclerosis*. 2009;204(2):440-446.
27. Cho AJ, Jung HY, Park HC, Oh J, Kim J, Lee YK. Relationship between abdominal aortic calcification on plain radiograph and coronary artery calcification detected by computed tomography in hemodialysis patients. *Clin Nephrol*. 2020;93(3):123-129.
28. Bolland MJ, Wang TKM, van Pelt NC, *et al*. Abdominal aortic calcification on vertebral morphometry images predicts incident myocardial infarction. *J Bone Miner Res*. 2010;25(3):505-512.
29. Lee DH, Steffes MW, Gross M, *et al*. Differential associations of weight dynamics with coronary artery calcium versus common carotid artery intima-media thickness: the CARDIA Study. *Am J Epidemiol*. 2010;172(2):180-189.
30. Kindblom JM, Bygdell M, Hjelmgren O, *et al*. Pubertal body mass index change is associated with adult coronary atherosclerosis and acute coronary events in men. *Arterioscler Thromb Vasc Biol*. 2021;41(8):2318-2327.
31. Pan XF, Yuan JM, Koh WP, Pan A. Weight change in relation to mortality in middle-aged and elderly Chinese: the Singapore Chinese Health Study. *Int J Obes (Lond)*. 2019;43(8):1590-1600.
32. Lee YB, Kim B, Park J, *et al*. Early mortality and cardiovascular disease, varied association with body mass index and its changes in insulin-treated diabetes: a nationwide study. *Int J Obes (Lond)*. 2021;45(11):2482-2489.
33. Ryu H, Hong Y, Kang E, *et al*; representing the KNOW-CKD Study Group. Rapid weight change over time is a risk factor for adverse outcomes in patients with predialysis chronic kidney disease: a prospective cohort study. *J Ren Nutr*. 2021;31(6):569-578.
34. French SA, Lutsey PL, Rosamond W, MacLehose RF, Cushman M, Folsom AR. Weight change over 9 years and subsequent risk of venous thromboembolism in the ARIC cohort. *Int J Obes (Lond)*. 2020;44(12):2465-2471.
35. Kisanuki K, Muraki I, Yamagishi K, *et al*; JPHC Study Group. Weight change during middle age and risk of stroke and coronary heart disease: the Japan Public Health Center-based Prospective Study. *Atherosclerosis*. 2021;322:67-73.
36. Li Y, Yu Y, Wu Y, *et al*. Association of body-weight fluctuation with outcomes in heart failure with preserved ejection fraction. *Front Cardiovasc Med*. 2021;8:689591.
37. Stevens J, Tyroler HA, Cai J, *et al*. Body weight change and carotid artery wall thickness. The Atherosclerosis Risk in Communities (ARIC) Study. *Am J Epidemiol*. 1998;147(6):563-573.
38. de Lima-Junior JC, Virginio VWM, Moura FA, *et al*. Excess weight mediates changes in HDL pool that reduce cholesterol efflux

capacity and increase antioxidant activity. *Nutr Metab Cardiovasc Dis*. 2020;30(2):254-264.
39. Makoundou V, Pataky Z, Bobbioni-Harsch E, Gachoud JP, Golay A. Do obese patients after weight loss become metabolically normal? *Obes Facts*. 2011;4(3):218-221.
40. Karason K, Wikstrand J, Sjöström L, Wendelhag I. Weight loss and progression of early atherosclerosis in the carotid artery: a four-year controlled study of obese subjects. *Int J Obes Relat Metab Disord*. 1999;23(9):948-956.
41. Kardassis D, Schönander M, Sjöström L, Karason K. Carotid artery remodelling in relation to body fat distribution, inflammation and sustained weight loss in obesity. *J Intern Med*. 2014;275(5):534-543.
42. Skilton MR, Sieveking DP, Harmer JA, *et al*. The effects of obesity and non-pharmacological weight loss on vascular and ventricular function and structure. *Diabetes Obes Metab*. 2008;10(10):874-884.
43. Cooper JN, Columbus ML, Shields KJ, *et al*. Effects of an intensive behavioral weight loss intervention consisting of caloric restriction with or without physical activity on common carotid artery remodeling in severely obese adults. *Metabolism*. 2012;61(11):1589-1597.
44. Tschoner A, Sturm W, Gelsinger C, *et al*. Long-term effects of weight loss after bariatric surgery on functional and structural markers of atherosclerosis. *Obesity (Silver Spring)*. 2013;21(10):1960-1965.
45. Feijóo-Bandín S, Aragón-Herrera A, Moraña-Fernández S, *et al*. Adipokines and inflammation: focus on cardiovascular diseases. *Int J Mol Sci*. 2020;21(20):7711.
46. Xiao X, Liu YZ, Cheng ZB, *et al*. Adipokines in vascular calcification. *Clin Chim Acta*. 2021;516:15-26.
47. Lehman SJ, Massaro JM, Schlett CL, O'Donnell CJ, Hoffmann U, Fox CS. Peri-aortic fat, cardiovascular disease risk factors, and aortic calcification: the Framingham Heart Study. *Atherosclerosis*. 2010;210(2):656-661.
48. Fox CS, Hwang SJ, Massaro JM, *et al*. Relation of subcutaneous and visceral adipose tissue to coronary and abdominal aortic calcium (from the Framingham Heart Study). *Am J Cardiol*. 2009;104(4):543-547.
49. Costa RM, Neves KB, Tostes RC, Lobato NS. Perivascular adipose tissue as a relevant fat depot for cardiovascular risk in obesity. *Front Physiol*. 2018;9:253.
50. Ong KL, McClelland RL, Rye KA, *et al*. The relationship between insulin resistance and vascular calcification in coronary arteries, and the thoracic and abdominal aorta: the Multi-Ethnic Study of Atherosclerosis. *Atherosclerosis*. 2014;236(2):257-262.
51. Carmo LS, Burdmann EA, Fessel MR, *et al*. Expansive vascular remodeling and increased vascular calcification response to cholecalciferol in a murine model of obesity and insulin resistance. *Arterioscler Thromb Vasc Biol*. 2019;39(2):200-211.
52. Li M, Qian M, Kyler K, Xu J. Adipose tissue-endothelial cell interactions in obesity-induced endothelial dysfunction. *Front Cardiovasc Med*. 2021;8:681581.
53. Aroor AR, Jia G, Sowers JR. Cellular mechanisms underlying obesity-induced arterial stiffness. *Am J Physiol Regul Integr Comp Physiol*. 2018;314(3):R387-R398.
54. Lovren F, Teoh H, Verma S. Obesity and atherosclerosis: mechanistic insights. *Can J Cardiol*. 2015;31(2):177-183.
55. Lee JS, Visser M, Tylavsky FA, *et al;* Health ABC Study. Weight loss and regain and effects on body composition: the Health, Aging, and Body Composition Study. *J Gerontol A Biol Sci Med Sci*. 2010;65(1):78-83.
56. Newman AB, Lee JS, Visser M, *et al*. Weight change and the conservation of lean mass in old age: the Health, Aging and Body Composition Study. *Am J Clin Nutr*. 2005;82(4):872-878; quiz 915-916.
57. Atkins JL, Wannamathee SG. Sarcopenic obesity in ageing: cardiovascular outcomes and mortality. *Br J Nutr*. 2020;124(10):1102-1113.
58. Ding C, Chan Z, Magkos F. Lean, but not healthy: the 'metabolically obese, normal-weight' phenotype. *Curr Opin Clin Nutr Metab Care*. 2016;19(6):408-417.
59. Kyulo NL, Knutsen SF, Tonstad S, Fraser GE, Singh PN. Validation of recall of body weight over a 26-year period in cohort members of the Adventist Health Study 2. *Ann Epidemiol*. 2012;22(10):744-746.
60. Stevens J, Keil JE, Waid LR, Gazes PC. Accuracy of current, 4-year, and 28-year self-reported body weight in an elderly population. *Am J Epidemiol*. 1990;132(6):1156-1163.