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Long-term Burden of Higher Body Mass Index and Adult Arterial Stiffness Are Linked Predominantly through Elevated Blood Pressure

Yang Liu[1,2], **Yinkun Yan**[2,3], **Xiangjun Yang**[1], **Shengxu Li**[4], **Lydia Bazzano**[2], **Jiang He**[2], and **Wei Chen**[2]

[1]Department of Cardiology, The First Affiliated Hospital of Soochow University, Suzhou, China

[2]Department of Epidemiology, Tulane University School of Public Health and Tropical Medicine, New Orleans, LA, USA

[3]Beijing Children's Hospital, Capital Medical University, National Center for Children's Health, Beijing, China

[4]Children's Minnesota Research Institute, Children's Hospitals and Clinics of Minnesota, Minneapolis, MN, USA

Abstract

Obesity and hypertension are important risk factors of arterial stiffness. However, the complex relationship between increased body mass index (BMI), elevated blood pressure (BP) and arterial stiffness is largely unknown. We aim to examine the mediation effect of elevated BP on the association of early life BMI, long-term burden and trend of BMI with arterial stiffness in midlife. The longitudinal study cohort consisted of 1,190 participants (829 whites and 361 blacks, 518 males, mean age=40.0 years at follow-up) who had been examined for BMI and BP 4–15 times from childhood and aortic-femoral pulse wave velocity (afPWV) in adulthood, with a mean follow-up period of 30.3 years. Total area under the curve (AUC_t) and incremental AUC (AUC_i) were calculated in random-effects models and used as long-term measures of BMI and BP. Total effects of BMI measures on adult afPWV, adjusted for covariates were all significant without adult BMI and systolic BP (SBP) measures included in the models. The mediation effects of adult SBP (20.2%) and SBP AUC_i (16.9%) were significant on the childhood BMI-afPWV association. Adult SBP showed significant mediation effects of 36.7% on the BMI AUC_i-afPWV association and 36.4% on the BMI AUC_t-afPWV association. The mediation effect of SBP AUC_i was estimated at 63.3% ($p<0.01$) on the BMI AUC_i-afPWV association. DBP had similar total and mediation effects. These findings suggest that the association of increased childhood BMI and its cumulative burden with adult arterial stiffness measured as afPWV is predominantly mediated through the long-term and increasing trend of BP.

Correspondence: Wei Chen, MD, PhD, 1440 Canal Street, Room 1504G, New Orleans, LA 70112, Tel: (504) 988-7611; Fax: (504) 988-7194, wchen1@tulane.edu.

DISCLOSURES

None.

Keywords

Body mass index; Blood pressure; Arterial stiffness; Mediation effect; Longitudinal study

INTRODUCTION

Arterial stiffening is an important independent risk factor of cardiovascular disease and starts many years before clinical manifestations of coronary artery disease, stroke and peripheral arterial disease.[1–3] It is well-known that obesity and hypertension play important roles in the development of arterial stiffness.[4,5] Extensive studies have shown that obesity plays an initial role in the process of vascular stiffening.[5–8] Elevated blood pressure (BP) is one of the accelerating risk factors for arterial stiffness in children and adults.[9] In a systematic review of 77 cross-sectional studies in adults, BP was consistently and independently associated with aortic pulse wave velocity (PWV).[10] Longitudinal cohort studies have shown that elevated BP in children and young adults is a strong predictor of arterial stiffness measures.[11–13] Despite overwhelming evidence for the association of obesity and BP with vascular stiffness, how obesity and elevated BP interact in accelerating the vascular stiffening process is unclear. Many studies found that the effect of overweight/obesity on PWV became nonsignificant when BP was included in the association analyses;[10] on the other hand, BP still remained significantly associated with arterial stiffness after adjustment for body mass index (BMI) in young adult life.[9,11] To date, the complex relationships between BMI, BP and arterial stiffness have not been elucidated.

BP levels and arterial stiffness measures are highly correlated and influenced by obesity and other cardiovascular risk factors during the development of hypertension.[12–14] Although the role of arterial stiffness in isolated systolic hypertension and pulse pressure amplitude has been well documented in the elderly population,[9,15,16] the Bogalusa Heart Study has shown that elevation of BP determines arterial stiffening instead of the other way around in a longitudinal cohort of young and middle-aged adults.[9] Existing observations on the close correlation between obesity and hypertension and their impact on vascular stiffness have raised a study question about whether obesity affects the arterial stiffening process directly or indirectly through the path of BP elevation. The current study aims to examine quantitatively the mediation effect of BP on the association of long-term burden and trends of increased BMI with adult arterial stiffness by utilizing a longitudinal cohort followed from childhood to adulthood in the Bogalusa Heart Study.

METHODS

All data and materials have been made publicly available at the NHLBI Biologic Specimen and Data Repository and can be accessed at https://biolincc.nhlbi.nih.gov/studies/bhs.

Study cohort

The Bogalusa Heart Study, founded by Dr. Gerald Berenson in 1973, is a series of long-term cardiovascular epidemiologic studies in a semi-rural, biracial (65% white and 35% black) community in Bogalusa, Louisiana. This study focuses on the early natural history of

cardiovascular disease from childhood.[17] Between 1973 and 2010, nine cross-sectional surveys of children aged 4–19 years and eleven cross-sectional surveys of adults aged 20–51 years, who had been previously examined as children, were conducted. These repeated cross-sectional surveys conducted every 2–3 years have resulted in serial observations from childhood to adulthood. The present longitudinal study cohort consisted of 1,190 adult subjects (829 whites and 361 blacks; 43.5% males; mean age=40.0 years in the last survey). These participants were examined 4–15 times for BMI and BP (at least 2 times in childhood and at least 2 times in adulthood) and aortic-femoral pulse wave velocity (afPWV) in adulthood. The mean follow-up period was 30.3 years (range=14.2–41.9 years) from the first childhood to the last adult survey.

All subjects in this study gave informed consent for each survey, and for those <18 years of age, consent of a parent/guardian was obtained. Study protocols were approved by the Institutional Review Board of the Tulane University Health Sciences Center (New Orleans, Louisiana).

General examinations

Standardized protocols were used by trained examiners across all surveys since 1973.[17] Replicate measurements of height and weight were made, and the mean values were used for analysis. BMI (weight in kilograms divided by height in meters squared) was used as a measure of overall adiposity.

Participants' BP levels were obtained on right arms in a relaxed sitting position by 2 trained observers (3 times each) between 8:00 AM and 10:00 AM. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded using a mercury sphygmomanometer. The fourth Korotkoff phase was used for DBP in children and the fifth Korotkoff phase was used for adults. The mean values of the 6 readings were used for analysis. For hypertensive patients (n=206) who were under anti-hypertensive treatment and had SBP/DBP<140/90 mmHg, forced values (140/90 mmHg) were assigned for measured SBP/DBP.

Aortic-femoral pulse wave velocity

Aortic-femoral pulse wave velocity (afPWV) was measured through a Toshiba digital ultrasound instrument (Xario SSA-660A; Toshiba America Medical Systems, Tustin, California). We placed a nondirectional transcutaneous Doppler flow probe (Toshiba PSK25AT, 2.5 MHz; Toshiba America Medical Systems) at the suprasternal notch, and put another probe (Toshiba PCK703AT, 7.5 MHz; Toshiba America Medical Systems) at the left femoral artery with the subject lying in a supine position. The output from the electrocardiogram and the 2 Doppler probes was displayed and recorded through a computer system. This system also recorded and stored the arterial flow waves from the 2 arterial sites and captured the output for subsequent scoring. After collection of the waveform data, we measured the distance between the aorta and femoral arteries with a caliper instrument to reduce the influence of body contours on the distance measured. The software averages the selected waveforms and determines the time from the R wave of the electrocardiogram to the foot of each waveform. The difference in timing between the 2 waves represents the time component of the velocity equation. We then calculated afPWV by dividing the distance

traveled by the time differential between the 2 waveforms.[18] To examine the reproducibility of afPWV, 46 randomly selected subjects were re-examined. The correlation between the 2 measurements was 0.91 on the same day and 0.68 on different days. The day-to-day variations were influenced by both measurement errors and physiological fluctuations.

Statistical methods

Long-term burden and trends of BMI and BP were measured as the area under the curve (AUC), which was calculated using statistical models we previously described.[19–21] In brief, growth curves of BMI and BP measured multiple times from childhood to adulthood were constructed using a random-effects model by SAS proc MIXED (SAS Institute Inc., Cary, North Carolina). A quadratic curve was fitted for BMI, and cubic curves for SBP and DBP in race-sex groups. The AUCs were calculated as the integral of the curve parameters during the follow-up period for each participant. Because participants had different follow-up years, the AUC values were divided by the number of follow-up years. The AUC measures as shown in Supplemental Figures S1 and S2 have advantages over other conventional longitudinal analysis models in that they measure both long-term burden and trends. Total AUC (AUC_t) can be considered a measure of a long-term cumulative burden; incremental AUC (AUC_i) determined by within-subject variability represents a combination of linear and nonlinear longitudinal trends.

Multivariable linear regression analyses were performed to examine the total effect (standardized regression coefficients, β) of BMI measures on adult afPWV, adjusted for race, sex, adult age, heart rate (HR), smoking and alcohol drinking. Race differences in the total effects were examined in linear regression interaction models by including race-BMI interaction terms, adjusted for covariates. Causal mediation analysis models were constructed as previously proposed by VanderWeele and Sobel.[22,23] In mediation analysis models with multiple mediators (Supplemental Figure S3), predictor variables (X) were childhood BMI, BMI AUC_t or BMI AUC_i; mediator variables (M) were adult BMI, adult BP, BP AUC_t or BP AUC_i; the outcome variable (Y) was adult afPWV. Four steps of the mediation analysis were involved in the calculation of the mediating effect:

Step 1: Showing that the predictor variable determines the outcome (Model $Y=cX$) (c=total effect).

Step 2: Showing that the predictor variable affects the mediators (Model $M_1=\beta_1 X$ and Model $M_2=\beta_3 X$) (β_1=indirect effect 1, β_3=indirect effect 3).

Step 3: Showing that the mediators determine the outcome controlling for the predictor (Model $Y=\beta_2 M_1 + \beta_4 M_2 + c'X$) ($\beta_2$=indirect effect 2, β_4=indirect effect 4, c'=direct effect).

Step 4: Calculating the proportion of mediation effects by $(\beta_1 \times \beta_2 / c) \times 100\%$ and $(\beta_3 \times \beta_4 / c) \times 100\%$.

In mediation analyses, testing the significance of the mediation effect is equivalent to testing the null hypothesis H_0: $\beta_2=0$ and/or $\beta_4=0$ versus the alternative hypothesis H_a: $\beta_2 \neq 0$ and/or $\beta_4 \neq 0$, using the procedures of R package mediation.[24] In the mediation models with childhood BMI as the predictor, two mediators (BP measures and adult BMI) were included

in the models. In the mediation models with BMI AUC_t or BMI AUC_i as the predictor, only one mediator (adult BP or BP AUC_i) was included in the models. Adult BMI could not be included in these models as a mediator because it was included in the calculation of BMI AUC measures.

RESULTS

Table 1 summarizes mean values (SD) of the study variables in childhood, adulthood and long-term measures of BMI and BP by race and sex. There were no significant differences in childhood BMI, SBP and DBP between race and sex groups; adult BMI, SBP and DBP showed significant race and sex differences except for race difference in BMI for males; adult HR showed significant sex difference in whites and race difference in males. Adult afPWV did not differ significantly between race and sex groups. Race and sex differences in AUC measures of BMI, SBP and DBP were all significant except for race difference in BMI AUC_t and BMI AUC_i in males.

Table 2 presents total effect of BMI measures on adult afPWV in linear regression models, adjusted for race, sex, adult age, HR, smoking and alcohol drinking. Adult afPWV was associated with childhood BMI (standardized regression coefficient, β=0.084, p=0.003), adult BMI (β=0.091, p=0.002), BMI AUC_t (β=0.088, p=0.002), and BMI AUC_i (β=0.079, p=0.005). When adult BMI, adult SBP, SBP AUC_t and SBP AUC_i were included in the models, respectively, for additional adjustment, the above associations became nonsignificant except for the BMI AUC_t-afPWV association with adjustment for SBP AUC_t. The effects of childhood and adult BMI, BMI AUC_t and BMI AUC_i on adult afPWV, adjusted for adult BMI, adult DBP, DBP AUC_t and DBP AUC_i were substantially similar to those with adjustment for SBP measures (Supplemental Table S1). Additional analyses were conducted to examine race differences in the total effects of BMI measures on adult afPWV (BMI-race interactions) adjusted for sex and other covariates. Although the total effects were weaker in blacks, the racial differences were not significant as indicated by the interaction P-values (all P>0.05). The results of racial differences in the total effects are presented in Supplemental Table S2.

Table 3 presents the results of mediation analyses of SBP measures and adult BMI on the childhood BMI-adult afPWV association, adjusted for race, sex, adult age, HR, smoking and alcohol drinking. The total effect of childhood BMI on adult afPWV (c=0.084, p<0.01) was estimated without SBP measures and adult BMI in the model. The mediation effects of adult SBP (20.2%, p<0.01) and SBP AUC_i (16.9%, p<0.01) were significant on the association between childhood BMI and adult afPWV. In all three models with SBP measures and adult BMI included, the direct effects of childhood BMI on adult afPWV were not significant. Of note, the associations between adult BMI and afPWV (β_4s) became nonsignificant when SBP measures included in the mediation models. In Supplemental Table S3, the mediation effect patterns of DBP were similar to those of SBP.

Figure 1 presents the mediation effect of adult SBP on the BMI AUC_i-adult afPWV association in a model with one mediator, adjusting for covariates. As mentioned above, adult BMI could not be included in the model as a mediator because it was included in the

calculation of BMI AUC_i. The total effect of BMI AUC_i on adult afPWV (c=0.079, p<0.01) was estimated without adult SBP in the model. The mediation effect of adult SBP on the BMI AUC_i-adult afPWV association was estimated at 36.7%, with a significant indirect effect (β_{Ind}=0.029, p<0.01). The direct effect (c'=0.050) was not significant.

Figure 2 presents the mediation effect of adult SBP on the BMI AUC_t-adult afPWV association in a one-mediator model without adult BMI. The total effect of BMI AUC_t on adult afPWV (c=0.088, p<0.01) was estimated without adult SBP in the model. The mediation effect of adult SBP on the BMI AUC_t-adult afPWV association was estimated at 36.4% (p<0.01). The direct effect (c'=0.056) was not significant.

Figure 3 shows the mediation effect of SBP AUC_i on the BMI AUC_i-adult afPWV association, adjusting for covariates. In this model, incremental AUCs of both BMI and SBP were included as the predictor and mediator, respectively. The mediation effect of SBP AUC_i on the BMI AUC_i-adult afPWV association increased to 63.3% (p<0.01), with a significant indirect effect (β_{Ind}=0.050, p<0.01). The direct effect (c'=0.029) was not significant.

Supplemental Figures S4-S6 show mediation effects of DBP measures on the BMI AUC-adult afPWV associations substantially similar to those of SBP measures.

DISCUSSION

Hypertension and obesity in children and adults are the most important risk factors related to arterial stiffening.[4–8] Extensive studies, including the Bogalusa Heart Study, have demonstrated that increased BMI since early life and elevated BP have an adverse effect on arterial stiffness.[6–10,12,25] It is well known that childhood obesity tracks into adulthood and associates with elevated adult BP.[26–28] Although it is widely accepted that childhood obesity affects arterial stiffness through adult BMI and BP, the degree of their mediation effects has never been reported, especially by using long-term BMI and BP measured from childhood to adulthood. In the present study, we quantified the mediation effect of adult BMI and BP and their long-term measures and found that the BMI-afPWV association was significantly mediated by adult BP and its long-term values, but not by adult BMI. The association between childhood BMI and adult afPWV was significantly mediated by adult BP (20.2% and 25.0%) and the increasing trends of BP measured by AUC_i (16.9%−21.4%). When long-term measures of both BMI and BP were used as the predictor and mediator, respectively, BP AUC_i showed considerably greater mediation effects (63.3% and 64.6%) than adult BP measured at one time-point on the association between BMI AUC_i and adult afPWV. These findings indicate that long-term burden of increased BMI from early life is associated with adult arterial stiffness predominantly through elevated BP, especially in terms of its long-term burden and trends.

Studies have indicated that childhood obesity is associated with adult cardiovascular morbidity and mortality.[29] The International Childhood Cardiovascular Cohort (i3C) Consortium found that obese children who were obese as adults had increased risks of type 2 diabetes, hypertension, dyslipidemia and carotid-artery atherosclerosis, but the risks of these outcomes among overweight/obese children who became nonobese by adulthood were

similar to those among persons who were never obese.[30] Other longitudinal cohort studies followed since childhood have also shown that obesity in both childhood and adulthood are associated with higher values of PWV.[5,7,8] These observations suggest that adult obesity is more important, and early life obesity might increase the future cardiovascular risk through later life obesity. Despite the strong tracking correlation of obesity measures from childhood to adulthood,[27,28,31] whether and in what degree the association between childhood obesity and adult arterial stiffness is mediated by adult body weight is largely unknown. We found in this study that although childhood BMI was strongly associated with adult afPWV, adult BMI had a marginally significant mediation effect (39.3%, p=0.061) on the association, and the mediation effect was substantially reduced with adjustment for BP in the models.

Elevated BP has been identified as the most important risk factor of vascular stiffness in enormous studies, including the Bogalusa Heart Study.[9–11,25] Based on our previous findings on the one-directional relation from BP to PWV in young and middle-aged adults,[9] a mediation analysis model was constructed in the present study with BP as the mediator in the indirect pathway from BMI to afPWV. We noted that adult BP had a significant mediation effect on the childhood BMI-afPWV association, adjusting for adult BMI, and a greater mediation effect on the association between long-term measures of BMI and adult afPWV. Of note, when the long-term increasing trend (AUC_i) of BMI was used as the predictor in the mediation analysis models, BP AUC_is had the strongest mediation effects (63.3% for SBP and 64.6% for DBP). In a systematic review of 77 cross-sectional studies in adults, BP was found to be consistently and independently associated with aortic PWV in 90% of studies.[10] The Bogalusa Heart Study has shown that elevated BP is one of the important risk factors of arterial stiffness measures in children and young adults.[9,13,25] Recently, the Cardiovascular Risk in Young Finns Study reported that individuals with elevated adult BP had an increased risk of high adult PWV, irrespective of childhood BP and independent of adult BMI.[11] Taken together, the evidence from the current and previous studies support the notion that increased adult BP plays a predominant role in mediating the obesity-arterial stiffness association.

This community-based longitudinal cohort provides an unparalleled opportunity to examine the mediation effects of BP in terms of both adult values and incremental trends in relation to BMI and afPWV. There were, however, a few limitations in this study. First, hypertensive subjects under pharmacological treatment represent a subgroup who would be expected to have the highest BP levels without treatment; the forced values of 140/90 mmHg assigned to the measured SBP/DBP for these hypertensive patients would result in some bias in the association and mediation analyses. Second, PWV can be reversed by long-term antihypertensive treatment; but, such an effect cannot be assessed without the PWV progression data in this study.

In conclusion, we demonstrated that increased BMI in childhood and adulthood and its life-long burden and incremental trends are all significantly associated with adult arterial stiffness measured as afPWV. The relationship between high BMI and increased afPWV is mainly through elevated BP. The long-term burden of elevated BP plays a more important role than adult BMI in mediating the vascular stiffening process in middle-aged adults. In

addition, the long-term measures of BP have stronger mediation effects on the association of cumulative burden and increasing trends of BMI with adult arterial stiffness.

PERSPECTIVES

The present study provides new insights into the life-long impact of BMI and BP on the arterial stiffening process and better understanding of the underlying mechanisms. These findings will help promote the development of new prevention and intervention strategies for controlling the modifiable predictors and mediators beginning in childhood to improve vascular health and reduce the risk of cardiovascular disease in later life.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS

afPWV	aortic-femoral pulse wave velocity
AUC_t	total area under the curve
AUC_i	incremental area under the curve
BMI	body mass index
BP	blood pressure
DBP	diastolic blood pressure
HR	heart rate
SBP	systolic blood pressure

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Novelty and Significance:

What Is New?

- The current study demonstrated that BMI in childhood and adulthood and its life-long burden and incremental trends are all significantly associated with adult arterial stiffness measured as aortic-femoral pulse wave velocity (afPWV).
- The association between high BMI and increased afPWV is mainly through long-term burden and trends of elevated blood pressure (BP).
- The long-term measures of BP have stronger mediation effects on the association of childhood BMI and its cumulative burden with adult arterial stiffness.

What Is Relevant?

The observations on the life-long impact of BMI and BP on the arterial stiffening process would improve our understanding of the underlying mechanisms. These findings will facilitate selection of new prevention and intervention strategies for controlling the modifiable predictors and mediators beginning in childhood to improve vascular health and reduce the risk of cardiovascular disease in later life.

Summary

Higher childhood and adulthood BMI and its life-long burden and incremental trends were all significantly associated with adult arterial stiffness measured as afPWV. The association between high BMI and increased afPWV was predominantly through elevated BP. The long-term burden of elevated BP played a more important role than adult BMI in mediating the vascular stiffening process in middle-aged adult life.

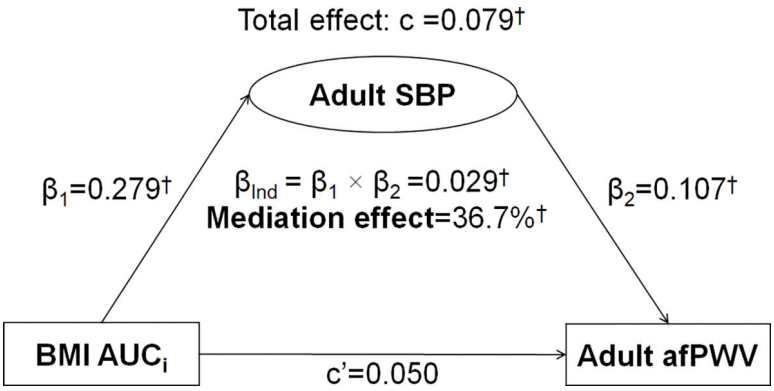

Figure 1.

Mediation Analysis Model of Adult SBP on the BMI AUC_i-afPWV Association

β, c and c' are standardized regression coefficients; c=total effect; c'=direct effect; β_1=indirect effect 1; β_2=indirect effect 2; β_{Ind}=total indirect effect; BMI=body mass index; SBP=systolic blood pressure; AUC_i=incremental area under the curve; afPWV=aortic-femoral pulse wave velocity

* P<0.05; † P<0.01

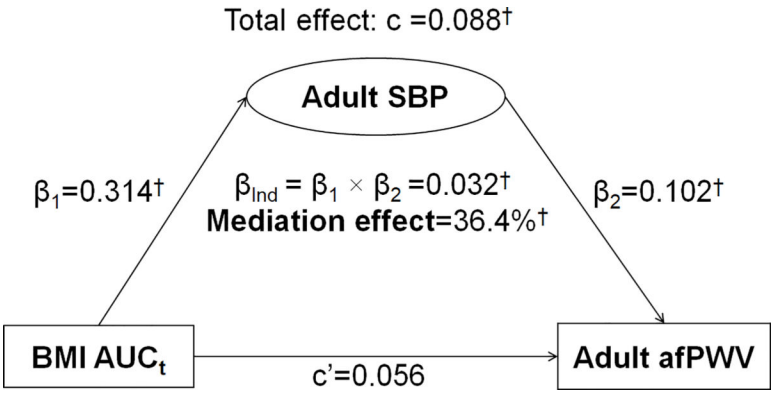

Figure 2.

Mediation Analysis Model of Adult SBP on the BMI AUC_t-afPWV Association

β, c and c' are standardized regression coefficients; c=total effect; c'=direct effect; β_1=indirect effect 1; β_2=indirect effect 2; β_{Ind}=total indirect effect; BMI=body mass index; SBP=systolic blood pressure; AUC_t=total area under the curve; afPWV=aortic-femoral pulse wave velocity

* P<0.05; † P<0.01

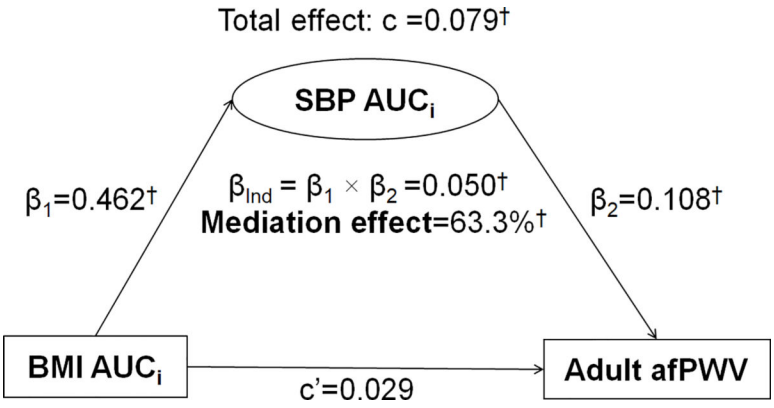

Figure 3.

Mediation Analysis Model of SBP AUC_i on the BMI AUC_i-afPWV Association

β, c and c' are standardized regression coefficients; c=total effect; c'=direct effect; β_1=indirect effect 1; β_2=indirect effect 2; β_{Ind}=total indirect effect; BMI=body mass index; SBP=systolic blood pressure; AUC_i=incremental area under the curve; afPWV=aortic-femoral pulse wave velocity

* P<0.05; † P<0.01

Table 1.

Characteristics of Study Participants by Race and Sex

Variable	White		Black		P for race difference	
	Male (n=375)	Female (n=454)	Male (n=143)	Female (n=218)	Male	Female
Childhood						
Age (y)	9.9 (3.3)	9.9 (3.4)	9.7 (3.0)	9.4 (2.9)	0.367	0.067
BMI (kg/m^2)	17.9 (3.6)	17.8 (3.7)	17.5 (3.5)	17.4 (3.6)	0.293	0.234
SBP (mmHg)	100.8 (10.0)	99.9 (9.8)	100.0 (11.8)	98.4 (10.2)	0.441	0.081
DBP (mmHg)	61.6 (8.1)	62.1 (8.5)	62.8 (8.5)	61.3 (8.7)	0.132	0.240
Adulthood						
Age (y)	40.4 (5.9)	40.0 (5.8)	40.4 (6.0)	39.3 (6.5)	0.987	0.125
BMI (kg/m^2)	30.2 (6.0) *	29.2 (7.4)	30.5 (8.0) *	32.7 (8.9)	0.685	<0.001
SBP (mmHg)	122.0 (12.8) †	114.3 (14.0)	132.2 (18.0) †	125.6 (19.1)	<0.001	<0.001
DBP (mmHg)	83.0 (8.1) †	77.9 (8.4)	88.9 (12.2) †	83.7 (11.7)	<0.001	<0.001
HR (beat/min)	68.3 (9.0) †	70.6 (9.0)	70.5 (9.8)	71.3 (9.2)	0.020	0.347
Smoker, n (%)	100 (26.7)	135 (29.7)	56 (39.2) *	62 (28.4)	0.006	0.729
Drinker, n (%)	128 (34.1)	184 (40.5)	29 (20.3) †	72 (33.0)	0.001	0.061
afPWV (m/s)	6.7 (4.3)	6.5 (4.5)	6.9 (2.5)	6.7 (3.0)	0.553	0.437
Long-term Measures						
Average age (y)	23.2 (5.1)	23.2 (4.9)	22.6 (4.9)	22.2 (4.5)	0.238	0.013
BMI AUC_t (kg/m^2)	25.4 (4.5) †	24.3 (5.1)	25.2 (5.5) *	26. 6 (5.9)	0.762	<0.001
BMI AUC_i (kg/m^2)	7.5 (2.9) †	6.7 (3.7)	7.7 (3.6) †	9.0 (4.3)	0.519	<0.001
SBP AUC_t (mmHg)	114.1 (7.7) †	108.4 (7.1)	118.3 (9.8) †	112.9 (9.0)	<0.001	<0.001
SBP AUC_i (mmHg)	13.3 (5.3) †	8.6 (5.8)	18.4 (7.6) †	14.3 (6.8)	<0.001	<0.001
DBP AUC_t (mmHg)	73.4 (5.6) †	70.9 (4.9)	75.4 (7.3) †	73.1 (6.3)	0.003	<0.001
DBP AUC_i (mmHg)	12.3 (3.4) †	9.2 (3.8)	13.6 (5.0) †	11.6 (4.5)	0.004	<0.001

Values are mean (SD) or n (%).

BMI=body mass index; SBP=systolic blood pressure; DBP=diastolic blood pressure; HR=heart rate; afPWV=aortic-femoral pulse wave velocity; AUC_t=total area under the curve; AUC_i=incremental area under the curve

Sex difference within racial groups:

*P<0.05;

†P<0.01

Table 2.

Linear Regression of Adult afPWV on BMI Measures since Childhood

Independent variable	β (95% CI)	P
Childhood BMI	0.084 (0.029 ~ 0.139)	0.003
Childhood BMI *	0.053 (−0.012 ~ 0.118)	0.107
Adult BMI	0.091 (0.034 ~ 0.148)	0.002
Adult BMI †	0.056 (−0.005 ~ 0.117)	0.069
BMI AUC_t	0.088 (0.033 ~ 0.143)	0.002
BMI AUC_t ‡	0.081 (0.020 ~ 0.142)	0.010
BMI AUC_i	0.079 (0.024 ~ 0.134)	0.005
BMI AUC_i §	0.030 (−0.033 ~ 0.093)	0.350

Race, sex, adult age, heart rate, smoking and alcohol drinking were included for adjustment.

*Additional adjustment for adult SBP and adult BMI

†Additional adjustment for adult SBP

‡Additional adjustment for SBP AUC_t

§Additional adjustment for SBP AUC_i

afPWV=aortic-femoral pulse wave velocity; BMI=body mass index; AUC_t=total area under the curve; AUC_i=incremental area under the curve; SBP=systolic blood pressure; β=standardized regression coefficient; CI=confidence interval

Table 3.

Mediation effect (standardized regression coefficient) of SBP measures and adult BMI on the childhood BMI-afPWV association

Effect	Model 1	Model 2	Model 3
Total effect (c)	0.084†	0.084†	0.084†
Mediator 1:	Childhood SBP	Adult SBP	SBP AUC_i
Direct effect (c')	0.052	0.053	0.056
β_1	0.396†	0.168†	0.135†
β_2	−0.003	0.101†	0.105†
β_{Ind}	−0.001	0.017†	0.014†
Mediation effect (%)	−1.2	20.2†	16.9†
Mediator 2:	Adult BMI	Adult BMI	Adult BMI
Direct effect (c')	0.052	0.053	0.056
β_3	0.525†	0.525†	0.525†
β_4	0.064	0.027	0.027
β_{Ind}	0.033	0.014	0.014
Mediation effect (%)	39.3	16.7	16.9

Race, sex, adult age, heart rate, smoking and alcohol drinking were included for adjustment.

c=total effect; c'=direct effect; β_1=indirect effect 1; β_2=indirect effect 2; β_3=indirect effect 3; β_4=indirect effect 4; β_{Ind}=total indirect effect. BMI=body mass index; SBP=systolic blood pressure; AUC_i=incremental area under the curve; afPWV=aortic-femoral pulse wave velocity

*P<0.05;

†P<0.01