Effects of Arterial Stiffness and Carotid Intima-Media Thickness Progression on the Risk of Overweight/Obesity and Elevated Blood Pressure/Hypertension: a Cross-Lagged Cohort Study

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ABSTRACT: We examined the temporal longitudinal associations of carotid-femoral pulse wave velocity (cfPWV), a measure of arterial stiffness, and carotid intima-media thickness (cIMT) with the risk of overweight/obesity and elevated blood pressure (BP)/hypertension. We studied 3862 adolescents aged 17–7 years from the Avon Longitudinal Study of Parents and Children, followed-up for 7 years. cfPWV and cIMT were measured by ultrasound. Total and trunk fat mass and lean mass were assessed by dual-energy X-ray absorptiometry. Body mass index and BP were measured. Data were analyzed using logistic regression, linear mixed-effect, and cross-lagged structural equation models, with covariate adjustments. Among 1719 male and 2143 female participants, higher cfPWV at 17.7 years was associated with the risk of elevated systolic BP/hypertension (odds ratio, 1.20 [1.02–1.41]; \( P = 0.026 \)), elevated diastolic BP/hypertension (1.77 [1.32–2.38]; \( P < 0.0001 \)), body mass index-overweight/obesity (1.19 [1.01–1.41]; \( P = 0.041 \)), and trunk fat mass overweight/obesity (1.24 [1.03–1.49]; \( P = 0.023 \)) at 24.5 years. Higher cIMT at 17.7 years had no associations with obesity and elevated BP at follow-up. cfPWV progression was directly associated with 7-year increase in systolic BP (effect estimate 16 mm Hg [9–24]; \( P < 0.0001 \)) and diastolic BP (28 mm Hg [23–34]; \( P < 0.0001 \)). cIMT progression was directly associated with the 7-year increase of all adiposity measures and diastolic BP. In the temporal analysis, baseline cfPWV was directly associated with follow-up systolic and diastolic BP, however, baseline BP was unassociated with follow-up cfPWV. cfPWV but not cIMT was bidirectionally associated with adiposity. Obesity and hypertension prevention from adolescence may require developing novel approaches to mitigate arterial stiffness. (Hypertension. 2022;79:159–169. DOI: 10.1161/HYPERTENSIONAHA.121.18449.)

Key Words: adolescent ◼ atherosclerosis ◼ blood pressure ◼ body mass index ◼ carotid-femoral pulse wave velocity ◼ obesity ◼ young adult

The global prevalence of obesity\(^1\) and hypertension\(^2\) in adolescence and young adulthood is on the rise. These twin risk factors of cardiovascular morbidity and mortality progress from childhood.\(^1\)–\(^6\) Although obesity, elevated blood pressure (BP), and hypertension are well-established risk factors for arterial stiffness and carotid intima-media thickness (cIMT), surrogate markers of atherosclerotic cardiovascular diseases, a temporal or bidirectional relationship remains unexamined among adolescents and young adults.\(^3\)–\(^5\),\(^7\)–\(^13\)

An American Heart Association’s scientific statement recommended that future studies investigate the natural history of arterial stiffness, obesity, and BP in relation to the rate at which arterial stiffness and BP increase with age.\(^4\) Similarly, another American Heart Association’s scientific statement just published recommended addressing the global burden of obesity hypertension...
Novelty and Significance

What Is New?
• The temporal longitudinal associations of repeatedly measured arterial stiffness (carotid-femoral pulse wave velocity) and carotid intima-media thickness with the risk of elevated blood pressure/hypertension and overweight/obesity risk among adolescents and young adults are unknown.

What Is Relevant?
• Adolescent arterial stiffness may be a precursor of hypertension and other metabolic risk factors in young adulthood rather than a consequence.

通过一种适合生命早期预防和控制的生活方式策略，特别是从年轻年龄开始，就非常重要的确定降低动脉僵硬度和cIMT从青少年人群中独立降低超重/肥胖和血压/高血压的关联至关重要。正是由于这一点，我们调查了从青春期至青年期持续测定的动脉僵硬度和cIMT的纵向关联。非标准缩写及缩略语

| ALSPAC | Avon Longitudinal Study of Parents and Children |
|--------|-------------------------------------------------|
| BMI    | body mass index                                 |
| BP     | blood pressure                                  |
| cfPWV  | carotid-femoral pulse wave velocity             |
| cIMT   | carotid intima-media thickness                  |
| OR     | odds ratio                                       |

学方法

数据可用性声明

数据的收集和管理

研究人群

非标准缩写及缩略语

新型和重要性

• 循环中测量的动脉僵硬度（cfPWV）和cIMT与青春期及青年期高血圧和超重/肥胖风险的纵向关联的关联度尚不明确。

• 青少年期动脉僵硬度可能是青春期后高血圧和其它代谢风险因素的前驱而不是后果。

在17.7岁时，持续高cfPWV与高血压/高血压和肥胖有强烈关联，表明肥胖和高血压的预防可能需要开发新的方法以减轻动脉僵硬度。
position, using a Vicorder instrument (Skidmore Medical, Bristol, United Kingdom) with 2 BP measurement channels and 2 Velcro pressure sensor cuffs applied over each of the carotid and femoral arteries. The cfPWV measurement was repeated until three readings that were within 0.5 m/s of each other had been recorded. The right and left common carotid arteries at age 24.5 years were imaged using an ultrasound machine (CardioHealth Panasonic and a 13.5 MHz linear array broadband transducer; probe; center frequency 9.0 MHz). We calculated BMI by dividing weight by squared height. Participants at >75th percentile of total fat mass, trunk fat mass, or having >24.9 kg/m² of BMI were classified as overweight and obese while those below this cut points were classified as normal weight. A high lean mass category included participants having >75th percentile of lean mass while those below this threshold were considered having normal lean mass. Participants were categorized as normotensive if BP was <120/80 mm Hg and elevated BP/hypertension when BP was >120/80 mm Hg. Missing data were handled with multiple imputations. Questionnaire to assess smoking behavior were administered at the 17.7-year and 24.5-year clinic visits. At the 17.7-year clinic visit, participants were briefly asked about their personal and family (mother, father, and siblings) medical history, such as a history of hypertension, diabetes, high cholesterol, and vascular disease. Moderate to vigorous physical activity at age 15.5 years was assessed with ActiGraphTM accelerometer worn for 7 days, whereas at 24.5 years moderate to vigorous physical activity was assessed using ActiGraph GT3X+ accelerometer device worn for 4 consecutive days; ideally starting the day after the clinic visit (see Supplemental Material and Tables S2 through S10).

Statistical Analysis

Participants’ descriptive characteristics were summarized as means and SD, medians, and interquartile ranges, or frequencies and percentages. We explored sex differences using independent t tests, Mann-Whitney U tests, or χ² tests for normally distributed, skewed or dichotomous variables, respectively. We assessed the normality of variables and logarithmically or reciprocally transformed skewed variables before further analysis.

We investigated the separate longitudinal associations of cfPWV and cIMT (predictors) at 17.7 years with each of total fat mass, trunk fat mass, lean mass, BMI, systolic BP, and diastolic BP (outcomes) categories at 24.5 years using logistic regression (Supplemental Methods). We also examined the separate associations of the 7-year progression in cfPWV and cIMT with the longitudinal progression in each of the outcomes from ages 17.7 through 24.5 years using linear mixed-effect models for repeated measures. Analyses were adjusted for sex, age at 17.7 years, and covariates measured at 17.7 and 24.5 years, such as low-density lipoprotein cholesterol, insulin, triglyceride, high-sensitivity C-reactive protein, high-density lipoprotein cholesterol, heart rate, fasting blood glucose, diastolic or systolic BP, and fat mass or lean mass depending on the outcome, smoking status, family history of hypertension/diabetes/high cholesterol/vascular disease, and moderate to vigorous physical activity at 15.5 and 24.5 years.

Lastly, we used structural equation modeling with autoregressive cross-lagged design (detailed in the Supplemental Material) to examine the separate temporal associations of cfPWV and cIMT with outcomes, adjusting for covariates listed above. All covariates were selected based on previous studies. We examined sex interactions and presented sex-stratified results and cross-sectional analysis results in Table S11. For sensitivity analyses, we examined the quartile categories (high, moderate-high, moderate-low, and low) of cfPWV and cIMT progression with the increase in body composition and BP and presented the result in Table S12. We considered differences and associations with a 2-sided P<0.05 as statistically significant and made conclusions based on effect estimates and their 95% CI or SEs. Analyses involving 40% of a sample of 10 000 ALSPAC children at 0.8 statistical power, 0.05 alpha, and 2-sided P value would show a minimum detectable effect size of 0.049 SDs if they had relevant exposure for a normally distributed quantitative variable. All statistical analyses were performed using SPSS statistics software, Version 27.0 (IBM Corp, Armonk, NY), and structural equation modeling was conducted using IBM AMOS version 27.0.

RESULTS

Study Population and Characteristics

Altogether, 14 901 children in the ALSPAC birth cohort were alive at 1 year of age, of whom 5217 adolescents participated in the 17.7-year follow-up clinic visit, whereas 4026 young adults participated in the 24.5-year follow-up clinic visit (Figure S1). Only 3862 participants who had complete cfPWV and cIMT measurements at age 17.7 years were included in the study. The prevalence of overweight/obesity at 17.7 and 24.5 years was 20% and 38%, respectively. The prevalence of elevated systolic BP/hypertension at 17.7 and 24.5 years was 26% and 33%, respectively. Other characteristics of our study participants are shown in Table 1 and Tables S7 through S10.

Longitudinal Associations of cfPWV and cIMT at 17.7 Years With Risk Categories of Obesity and Hypertension at Age 24.5 Years

A higher cfPWV at 17.7 years predicted elevated systolic BP/hypertension (odds ratio [OR], 1.20 [95% CI, 1.02–1.41]; P=0.026), elevated diastolic BP/hypertension (OR, 1.77 [95% CI, 1.32–2.38]; P<0.0001), BMI- overweight/obesity (OR, 1.19 [95% CI, 1.01–1.41]; P=0.041), trunk fat mass-obesity (OR, 1.24 [95% CI, 1.03–1.49]; P=0.023), and decreased high lean mass (OR, 0.73 [95% CI, 0.54–0.98]; P=0.035) at age 24.5 years, after adjusting for cardiometabolic and lifestyle factors (Table 2). Among males, a higher cfPWV at 17.7 years predicted elevated systolic BP/hypertension (OR, 1.31 [95% CI, 1.02–1.70]; P=0.038) and elevated diastolic BP/hypertension (OR, 2.18 [95% CI, 1.49–3.19]; P<0.0001) at 24.5 years but not among females (OR, 1.09 [95% CI, 0.83–1.42]; P=0.542) and (OR, 1.40
Effect of cfPWV and cIMT Progression on Fat Mass, Lean Mass, and BP Progression From Ages 17.7 to 24.5 Years

A 7-year progression in cfPWV was directly associated with the 7-year increase in lean mass: (mean difference from baseline to follow-up 0.11 kg; [95% CI, 0.06–0.15; P<0.001]), systolic BP: 16 mm Hg; (9–24; P<0.0001), and diastolic BP: 28 mm Hg; (23–34; P<0.0001).
<0.0001) but negatively associated with trunk fat mass −0.19 kg (−0.35 to −0.02; $P<0.0001$) and BMI: −0.05 kg/m$^2$; (−0.09 to −0.01; $P=0.026$), after adjustment for cardiometabolic and lifestyle factors (Table 3). The sex-stratified results were largely in consonance with the combined results (Table 3). Additional adjustments for light physical activity and sedentary time did not alter the results (data not shown). In the sensitivity analyses with the lowest quartile as the reference, the highest quartile of cfPWV progression from 17.7 through 24.5 years was directly associated with the 7-year increase in total fat mass, trunk fat mass, and BMI (Table S12). In comparison with the lowest or reference category, the highest quartile of cfPWV progression was associated with the 7-year increase in systolic BP: 4 mm Hg; (3–5; $P<0.0001$) and diastolic BP: 3 mm Hg; (2–4; $P<0.0001$). The moderate-high cfPWV quartile was associated with the 7-year increase in systolic BP: 3 mm Hg; (1–4; $P<0.0001$) and diastolic BP: 2 mm Hg; (1–3; $P<0.0001$). The moderate-low cfPWV quartile was associated with the 7-year increase in systolic BP: 2 mm Hg; (1–3; $P=0.001$) and diastolic BP: 1 mm Hg (0.4–2; $P=0.002$; Table S12).

A 7-year cIMT progression was directly associated with the 7-year increase in total fat mass, trunk fat mass, BMI, lean mass, and diastolic BP but negatively associated with systolic BP after adjustment for cardiometabolic and lifestyle factors (Table 3). Among males, there were no associations between cIMT progression and increase in lean mass and systolic BP. However, among females, cIMT progression was not associated with trunk fat mass and diastolic BP (Table 3). In the sensitivity analyses with the lowest quartile as the reference, the highest quartile of cIMT progression from 17.7 through 24.5 years was directly associated with the 7-year increase in lean mass and systolic BP but not associated with the increase in total fat mass, trunk fat mass, BMI, and diastolic BP (Table S12).

**Cross-Lagged Temporal Relationships of cfPWV and cIMT With Fat Mass, Lean Mass, and BP**

cfPWV, total fat mass, trunk fat mass, BMI, lean mass, systolic, and diastolic BP at 17.7 years were directly associated with their individual variables at 24.5 years; however, cIMT at 17.7 years was inversely associated with cIMT at 24.5 years (Table 4). We observed bidirectional associations between cfPWV and all measures of body composition, whereas cIMT had bidirectional associations with lean mass but had no relationships with adiposity indices (Figure 1A and 1B and Table 4). Higher cfPWV at 17.7 years was associated with high systolic and diastolic BP at 24.5 years, but neither systolic nor diastolic BP at 17.7 years was associated with cfPWV at 24.5 years (Figure 2A and Table 4). cIMT at 17.7 years was unrelated to systolic and diastolic BP at 24.5 years, whereas only diastolic BP at 17.7 years was associated with cIMT at 24.5 years (Figure 2B and Table 4).

**DISCUSSION**

In a large longitudinal birth cohort, we showed for the first time that arterial stiffness, assessed by cfPWV, and cIMT during adolescence may be independent risk factors for obesity and incident hypertension in early adulthood. We thus conclude because first, we observed that cfPWV at 17.7 years independently predicted general and trunk obesity, decreased lean mass,
and elevated BP/incident hypertension at 24.5 years. Second, we reported that a 7-year increase in cfPWV was directly associated with the 7-year increase in systolic BP and diastolic BP, whereas the longitudinal progression of cIMT was directly associated with the 7-year increase in total fat mass, trunk fat mass, lean mass, and diastolic BP. Lastly, using cross-lagged temporal structural equation models, cfPWV was bidirectionally associated with total fat mass, trunk fat mass, and lean mass but temporally preceded systolic and diastolic BP. cIMT was bidirectionally associated with lean mass only.

**Arterial Stiffness with Obesity, Lean Mass, and Incident Hypertension**

We and others have shown that cumulative exposure to total fat mass from childhood was associated with cfPWV in adolescence and in young adulthood. These previous findings and a meta-analysis involving 2237 children/adolescents (1281 with obesity, 956 healthy BMI controls) between 5 and 24 years of age emphasize a unidirectional relationship in which obesity is a strong and independent risk factor for arterial stiffness. However, to the best of our knowledge, it remains unknown whether arterial stiffness precedes (temporal relationship) incident obesity among a healthy young population. Our prospective analysis revealed that cfPWV at 17.7 years was independently associated with ≈20% increased risk of total and trunk fat mass overweight/obesity at age 24.5 years, although the 7-year increase in cfPWV was unrelated to the 7-year increase in total fat mass and trunk fat mass. Nonetheless, the cross-lagged findings showed that cfPWV had strong bidirectional associations with all measures of adiposity, suggesting that cfPWV may be a cause and a consequence of altered fat metabolism and deposit since increased arterial stiffness leads to high-flow low-resistance microvascular organ damage in the liver, pancreas, etc. By contrast, we observed that a higher cfPWV in late adolescence predicted 25% reduced lean mass in early adulthood. We have shown that higher lean mass from age 9 to 24 years may drive the increase in cfPWV from 17 to 24 years and in tandem with the cross-lagged findings, bidirectional relationships likely exist between cfPWV and muscle mass. In adults, arterial stiffness has been related to decreased lean mass via the mechanism of aging-induced chronic inflammation, hormonal dysregulation, impaired glucose metabolism, and other comorbidities.

There is mounting evidence on the bidirectional relationship between arterial stiffness and BP and that arterial stiffness predates altered BP in the causal pathway. We have shown that BP is independently associated with higher cfPWV where a 15-year 1 mm Hg rise in BP predicted a 0.013 m/s rise in cfPWV over a 7-year period. For the first time, we found in a young population, across cross-sectional, longitudinal, and cross-lagged analyses that arterial stiffness, measured with cfPWV, is a strong and consistent independent predictor of elevated BP/incident systolic and diastolic hypertension. We observed that a 1 m/s increase in cfPWV from ages 17.7 to 24.5 years was associated with a 4 mm Hg and 3 mm Hg increase in systolic and diastolic BP, respectively, over 7 years among participants in the highest quartile of cfPWV. Importantly, the cross-lagged findings suggest that arterial stiffness in late adolescence precedes the increase in systolic and diastolic BP in early adulthood.

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**Table 3. Longitudinal Progression in Arterial Stiffness and Carotid Intima-Media Thickness in Relation to Progression in Fat Mass, Lean Mass, and Blood Pressure From Age 17.7 to 24.5 y**

| Measure                        | Total fat mass (kg) | Trunk fat mass (kg) | Lean mass (kg) |
|--------------------------------|--------------------|--------------------|----------------|
|                                 | Effect estimate (95% CI) | P value | Effect estimate (95% CI) | P value | Effect estimate (95% CI) | P value |
| All participants (n=3862)      |                    |                |                      |
| Carotid-femoral pulse wave velocity | −0.072 (−0.219 to 0.075) | 0.338 | −0.185 (−0.350 to −0.020) | 0.028 | 0.106 (0.063 to 0.149) | <0.0001 |
| Carotid intima-media thickness | 0.096 (0.079 to 0.111) | <0.0001 | 0.061 (0.042 to 0.080) | <0.0001 | 0.024 (0.019 to 0.028) | <0.0001 |
| Male participants (n=1719)     |                    |                |                      |
| Carotid-femoral pulse wave velocity | −0.121 (−0.382 to 0.141) | 0.365 | −0.212 (−0.486 to 0.062) | 0.129 | 0.092 (0.034 to 0.151) | 0.002 |
| Carotid intima-media thickness | 0.158 (0.131 to 0.185) | <0.0001 | 0.133 (0.102 to 0.163) | <0.0001 | 0.006 (−0.004 to 0.016) | 0.243 |
| Female participants (n=2143)   |                    |                |                      |
| Carotid-femoral pulse wave velocity | −0.008 (−0.159 to 0.144) | 0.923 | −0.139 (−0.323 to 0.045) | 0.139 | 0.093 (0.035 to 0.152) | 0.002 |
| Carotid intima-media thickness | 0.031 (0.014 to 0.049) | 0.001 | −0.006 (−0.027 to 0.016) | 0.610 | 0.027 (0.020 to 0.034) | <0.0001 |

*Continued*
Table 3. Continued

| Body mass index (kg/m²) | Systolic blood pressure (mm Hg) | Diastolic blood pressure (mm Hg) |
|------------------------|---------------------------------|---------------------------------|
| Effect estimate (95% CI) | P value | Effect estimate (95% CI) | P value | Effect estimate (95% CI) | P value |
| −0.050 (−0.094 to −0.006) | 0.026 | 16.160 (8.841 to 23.839) | <0.0001 | 28.151 (22.520 to 33.781) | <0.0001 |
| 0.018 (0.013 to 0.022) | <0.0001 | −1.540 (−2.512 to −0.568) | 0.002 | 1.099 (0.363 to 1.835) | 0.003 |
| −0.080 (−0.138 to −0.022) | 0.007 | 12.828 (8.825 to 24.430) | 0.036 | 28.880 (20.226 to 37.533) | <0.0001 |
| 0.020 (0.013 to 0.027) | <0.0001 | −0.552 (−2.215 to 1.111) | 0.514 | 2.966 (1.762 to 4.169) | <0.0001 |
| −0.026 (−0.089 to 0.037) | 0.417 | 18.140 (8.127 to 28.152) | <0.0001 | 27.968 (20.617 to 35.320) | <0.0001 |
| 0.015 (0.007 to 0.022) | <0.0001 | −1.782 (−2.984 to −0.580) | 0.004 | 0.153 (−0.784 to 1.091) | 0.748 |

Multivariable analysis was adjusted for sex only in all participants’ model, age at 17.7 y, and covariates at 17.7 and 24.5 y such as low-density lipoprotein cholesterol, insulin, triglyceride, high-sensitivity C-reactive protein, high-density lipoprotein cholesterol, heart rate, fasting blood glucose, diastolic or systolic blood pressure and fat mass or lean mass depending on the outcome, moderate to vigorous physical activity at 15.5 y, smoking status, and family history of hypertension/diabetes/high cholesterol/vascular disease. Skewed variables were logarithmically transformed before analyses. Effect estimate was from linear mixed-model analyses for repeated measures. P<0.05 was considered statistically significant.

predict elevated systolic and diastolic BP/hypertension at follow-up when controlled only for sex but was statistically significant after controlling for several potential confounders. This suggests that logistic regression analyses may be reported alongside path analysis or linear regression hierarchical models for the robustness of the results. Our findings, therefore, shed novel insights into the natural history of arterial stiffness and BP in relation to the rate at which arterial stiffness and BP increase with age, as identified as a research priority by the American Heart Association.4,13 Taken together, our finding buttress previous reports4,5,13 that arterial stiffness antedates and probably contribute to the pathogenesis of incident hypertension, independent of cardiometabolic, and lifestyle factors. The carotid-femoral artery has a thin collagenous adventitial layer, an elastin-laden medial layer, and a thin intimal layer.4,5,8,27 The elastic media layer enables arterial distensibility during systole and blood flow augmentation during diastole. Elastic fiber degradation or an increased collagen deposit reduces the energy storing capacity of the elastic fiber and decreases collagen fiber undulation, thereby occasioning stiffened arteries.4,5,8,27 Arterial stiffening may lead to the remodeling of small resistance arteries which are implicated in the early phases of prehypertension. Damage to these arteries results in an elevated BP via wave reflections and propagation and may progressively aggravate into a vicious loop of increased arterial stiffness and more pressure wave reflections.4,5,8,27 Arterial stiffening increases characteristic impedance leading to higher wave reflections and pulse pressure propagation. This reflected wave returns earlier during ventricular contraction and increases late systolic BP.4,5,27

Carotid Intima-Media Thickness with Obesity, Lean Mass, and Incident Hypertension

Recent reports among adolescents10 and young adults12,24 seem to challenge the previous notion that obesity measured by BMI predicts cIMT progression in a healthy young population.9 These reports10,12,24 in a large healthy young population, emphasized that dual-energy X-ray absorptiometry–measured total fat mass or trunk fat mass may not associate with cIMT progression during early life. Nonetheless, evidence on whether cIMT has a temporal relationship with body fat is lacking. In the longitudinal analysis, higher cIMT at 17.7 years of age had no relationship with all measures of adiposity at 24.5 years, both in the logistic regression and cross-lagged analyses. However, a 7-year progression in cIMT was independently and directly associated with the 7-year increase in total and central adiposity, especially in males. As expected, males had lower body fat content in contrast to females; however, there was a significant accumulation of fat mass among males during the 7-year growth. The median 7-year increase in total fat mass and trunk fat mass among males was 7.63 kg and 3.49 kg, respectively, whereas females had 2.88 kg of total fat mass and 0.45 kg of trunk fat mass increase. This 3- to 8-fold increase in fat mass among males relative to females may be a simultaneous increase not in the causal pathway of cIMT progression since cIMT increase did not precede the fat mass increase in the cross-lagged analyses.
We observed that the 7-year progression in cIMT was directly associated with the increase in lean mass from ages 17.7–24.5 years in both males and females, consistent with cross-sectional and cross-lagged analysis. In adolescents\textsuperscript{10} and young adults,\textsuperscript{12,24} cumulative high exposure to a dual-energy X-ray absorptiometry–measured lean mass was directly associated with cIMT\textsuperscript{10,24} and cIMT progression,\textsuperscript{24} but little is known regarding a reverse association (temporal association).\textsuperscript{38} We have now shown that a bidirectional relationship exists between cIMT and lean mass in a young healthy population, although the relationship is stronger when lean mass is the predictor. This temporal relationship may be due to a physiological carotid wall adaptation in association with skeletal muscle growth during maturation.\textsuperscript{10,24,26} It is important to note that higher cIMT at 17.7 years predicted a slight decrease in lean mass at 24.5 years. Considering the age and health status of our study population, an optimal cIMT may facilitate, decreased reactive oxidant species, rapid oxygen supply, increased myocyte proliferation, and increased production of anabolic hormones.\textsuperscript{10,28}

cIMT measured at 17.7 years was unrelated to systolic or diastolic BP at 24.5 years either via logistic regression or cross-lagged analyses. However, a 7-year cIMT progression was independently and directly associated with the 7-year increase in diastolic BP, particularly among males. Although cIMT maximally increased by ≈18% of the increase in diastolic BP during the observation period. This simultaneous rise in cIMT and intravascular pressure may suggest a compensatory nonatherosclerotic adaptation occurring between lumen diameter and cIMT via the maintenance of local wall shear stress.\textsuperscript{39}

### Strengths and Limitations of the Study

The ALSPAC dataset based on a large birth cohort provides an extensive array of gold-standard and repeated...
measures of variables during adolescence and young adulthood which allowed us to construct cross-lagged structural equation models to examine temporal and bidirectional associations. We could not adjust for diet as the variable was unavailable at 17.7- and 24.5-year follow-up clinic visits, nonetheless, participants’ body composition and metabolic state which we controlled for may reflect their diets. The absolute time in moderate to vigorous physical activity was a relatively small proportion of the day, although within the expected range. Therefore, we additionally controlled for sedentary time and light physical activity but the findings remained unchanged. We cannot exclude unmeasured or residual confounders, for instance, adiponectin has been associated with arterial stiffness progression. There were no regional differences in our study population as all were from the Avon area of England and were mostly White participants; therefore, we are unable to generalize our findings to other populations with different ethnicities. Lastly, the observational nature of our study may not establish causality; however, a temporal longitudinal path in the associations of cfPWV and cIMT with obesity and hypertension is a critical step in the causal pathway.

**PERSPECTIVES**

Adolescence arterial stiffness independently predicted trunk fat overweight/obesity, elevated BP/incident hypertension, and a decreased lean mass in early adulthood. Arterial stiffness appears to precede the increase in systolic and diastolic blood pressure:
diastolic BP but the relationship with adiposity may be more complex and bidirectional. Increased cIMT at 177 years was associated with decreased lean mass at 24.5 years. A 7-year arterial stiffness progression, that is, persistently high cfPWV from 177 through 24.5 years, was strongly associated with the increase in systolic and diastolic BP, whereas cIMT progression was associated with the increase in all measures of adiposity at the end of the observation period. Reducing arterial stiffness and cIMT from adolescence may be effective in preventing elevated BP/hypertension and overweight/obesity risks in early adulthood. Nonetheless, future temporal longitudinal investigations of cfPWV and cIMT in mediating obesity and hypertension risk are warranted in a large multiethnic adolescent population.

ARTICLE INFORMATION
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Disclosures
None.

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