**Body silhouette trajectories across the lifespan and vascular aging: The Paris Prospective Study 3**

Thomas T van Sloten, MD, PhD[1-4], Pierre Boutouyrie, MD, PhD[1,3,5], Quentin Lisan, MD[1,2], Muriel Tafflet, MSc[1,2], Frédérique Thomas, PhD[6], Catherine Guibout, PhD[1,2], Rachel E Climie, PhD[1,2,7,8], Bruno Pannier, MD[6], James E Sharman, PhD[1,7], Stéphane Laurent, MD, PhD[1,3,5], Xavier Jouven, MD, PhD[1,2], Jean-Philippe Empana, MD, PhD[1,2]

1. Université Paris Descartes, Sorbonne Paris Cité, Faculté de Médecine, Paris, France.
2. INSERM, UMR-S970, Paris Cardiovascular Research Center, Department of Epidemiology, Paris, France.
3. INSERM, UMR-S970, Paris Cardiovascular Research Center, Department of Arterial Mechanics, Paris, France.
4. Cardiovascular Research Institute Maastricht and Department of Internal Medicine, Maastricht University Medical Centre, Maastricht, the Netherlands
5. AP-HP, Georges Pompidou European Hospital, Department of Pharmacology, Paris, France.
6. Preventive and Clinical Investigation Center, Paris, France.
7. Menzies Institute for Medical Research, University of Tasmania, Hobert, Australia
8. Baker Heart and Diabetes Institute, Melbourne, Australia

**Running title:** Lifetime body silhouettes and vascular aging
**Word count**: 5,933
**Table:** 3
**Figures:** 3

**Address for correspondence:**
Thomas van Sloten, INSERM U970, Paris Cardiovascular Center, 56 rue Leblanc, 75015 Paris, France, E:t.van.sloten@mumc.nl; T:+33-153987961

Abstract

Vascular aging is a major contributor to cardiovascular disease, and can be quantified by higher carotid stiffness, intima-media thickness and diameter, and hypertension. Weight gain across the lifetime may be an important, modifiable determinant of vascular aging. We therefore aimed to assess lifetime body silhouette trajectories (a marker of weight change across the lifespan) in relation to vascular aging in late adulthood. We used cross-sectional data from a community-based cohort study (n=8,243/age 59.4/38.7% women). A linear mixed model was used to assess trajectories of recalled body silhouettes from age 8-45. We assessed carotid artery properties (ultrasonography), resting hypertension (blood pressure ≥140/90 mmHg or use of antihypertensives), and exaggerated exercise blood pressure, a marker of masked hypertension (systolic blood pressure ≥150 mmHg during submaximal exercise) at study recruitment when the participants were aged 50 to 75. We identified five distinct body silhouette trajectories: lean-stable (32.0%), lean-increase (11.1%), moderate-stable (32.5%), lean-marked increase (16.3%) and heavy-stable (8.1%). Compared to individuals in the lean-stable trajectory, those in the moderate-stable, lean-marked increase and heavy-stable trajectories had higher carotid stiffness, intima-media thickness and diameter (odds ratios between 1.23-2.10 for highest quartile vs. lowest quartile of manifestations of vascular aging, P<.05), and were more likely to have resting hypertension and exaggerated exercise blood pressure, after adjustment for potential confounders (odds ratios between 1.31-1.60, P<.05). Vascular aging was most prominent among individuals who were lean in early life but markedly gained weight during young adulthood, and among those who were heavy in early life and maintained weight.

Keywords. arterial stiffness, intima-media thickness, hypertension, adiposity, life course

## Introduction

Vascular aging, i.e. accumulation of functional and structural changes of vessels throughout life, is a major contributor to cardiovascular disease.[1] Key manifestations of vascular aging include arterial stiffening, higher carotid intima-media thickness (IMT), carotid diameter enlargement, and higher blood pressure (BP) at rest (resting hypertension) or during exercise (exaggerated exercise BP, a marker of masked hypertension that is otherwise missed by resting BP values[2]). These manifestations have all been associated with incident cardiovascular disease.[2-5] Beyond the effect of age, vascular aging can be accelerated by exposure to poor lifestyle across the lifespan, and, thus, may be a partly modifiable process.[6]

Given the global burden of obesity, understanding the effect of adiposity on vascular aging is of critical importance. Evidence is currently incomplete, as most previous studies,[7-15] but not all,[16] have focused on adiposity only at specific age periods, i.e. adulthood[7-12] or childhood/adolescence into young adulthood.[13-15] Adiposity is, however, a dynamic and changing process starting early in life, i.e. body mass index typically increases with age, in particularly in young adulthood,[17] and childhood obesity is often tracked into adulthood.[18] A life course approach is, therefore, crucial to study the effect of adiposity on vascular aging. This will help to develop effective prevention strategies targeting the life period at which adiposity has a predominant influence on vascular health.[6]

Recalled body silhouettes at different ages have a moderate to good correlation with objectively measured adiposity at these different ages (see supplemental material Table S1 for a summary of previous studies).[19-22] By combining recall of body silhouettes at different ages it is possible to construct body silhouette trajectories over the life course.[23] Using this

approach, body silhouettes trajectories have been shown to be associated with a higher incidence of type 2 diabetes[24, 25] and cardiovascular disease,[25] and higher mortality.[23]

We therefore calculated body silhouettes trajectories over the life course using self-recalled body silhouettes from age 8 up to 45 and quantified their association with vascular aging in late adulthood.

## Methods

Data are available on request subject to approval by the Paris Prospective Study 3 (PPS3) scientific committee.

### Study population

The PPS3 (n=10,157) is a community-based cohort study on novel markers for phenotypes of cardiovascular disease, as described previously.[26] In brief, individuals aged between 50-75 years were recruited at the Centre d'Investigations Préventives et Cliniques, a large preventive medical center in Paris (France), between June, 2008 and June, 2012. The Ethics Committee of the Cochin Hospital (Paris, France) approved the study. PPS3 was registered in the World Health Organization international clinical trial registry platform (NCT00741728).

### Body silhouettes

We used body silhouettes adapted from Stunkard et al.[27] At study recruitment, participants self-reported one of the seven pictorial body diagrams (somatotypes) (Figure 1) that best depicted their body silhouette at ages 8, 15, 25, 35 and 45 years.

### Manifestations of vascular aging

*Carotid stiffness, IMT and diameter*

Carotid stiffness (i.e. carotid distensibility coefficient [DC] and Young's elastic modulus, [YEM]), IMT and diameter were determined using high-resolution echotracking as described previously and further detailed in the online supplemental material.[28] Carotid DC represents arterial stiffness and carotid YEM the stiffness of the arterial wall material at operating pressure. Please note that lower values of carotid DC, but higher values of carotid YEM reflect greater arterial stiffness.

*Resting hypertension and exaggerated exercise BP*

Resting BP was recorded in triplicate using an Omron 705 C oscillometric device and an appropriate sized cuff after 10 min of supine rest, as described previously.[29] The mean of the last two measurements were used in the analysis. Resting hypertension was defined by a BP of ≥140/90 mmHg and/or use of antihypertensive medication. In addition, BP was measured during a submaximal exercise step test.[29] After the resting BP measurements, participants performed the step test with the BP cuff left in situ to enable recording of one BP measurement in the shortest time immediately after participants had stopped exercise. The exercise test consisted of stepping up and down two steps for 2 min at your own pace. Exaggerated exercise BP was defined as an exercise systolic BP ≥150 mmHg irrespective of the use of antihypertensive medication.[29]

Covariates

A self-administered questionnaire was used to obtain information on education level, smoking behavior (never, former and current), depressive symptoms, physical activity, medication use, medical history, birth weight (categories <2.5 kg, 2.5-4 kg, and >4kg; data on exact birth weight were not available) and dietary habits. We divided education level into three categories: 1) low (no or primary education); 2) intermediate (secondary education), and 3) high (higher education or university). The validated Baecke score was used to estimate overall physical activity (higher scores indicating higher levels of physical activity).[30] Dietary habits were evaluated using a semi-quantitative 18-item food frequency questionnaire.[31] We considered the following dietary habits, as defined previously[31]: habitual breakfast (complete breakfast vs. no complete breakfast), consumption of fish/week (>4 times vs. ≤3 times), consumption of fresh fruit/week (>4 times vs. ≤3 times) and consumption of vegetables/week (>4 times vs. ≤3 times). Depression symptoms were assessed using the 13-items

Questionnaire of Depression 2nd version, Abridged (QD2A).[32] We defined the presence of depressive symptoms by a QD2A score ≥7 or use of antidepressant medication. Prior cardiovascular disease was defined by a self-reported history of stroke, myocardial infarction and/or angina pectoris, and diabetes by use of glucose-lowering medication or a fasting blood glucose ≥7 mmol/L.

Analytical sample

Of the 10,157 participants, 539 individuals (5.3%) had missing data on body silhouettes at all ages, 95 (0.9%) on four ages, 150 on three ages (1.5%), 138 (1.4%) on two ages and 533 (5.2%) on one age. A total of 8,702 (85.7%) individuals had no missing data. We calculated the trajectories in all individuals (n=9,020, 88.8%) with available data on body silhouettes on ≥three out of the five ages and including the earliest (8 years) and the latest age (45 years). In addition, 777 individuals had missing data on manifestations of vascular aging. The final study sample therefore consisted of 8,243 individuals. Excluded participants as compared to those included in the present analysis had a more unfavorable cardiovascular risk profile (see online supplemental material).

Statistical analysis

Analyses were performed using SAS version 9.4. The percentage of missing values with regard to potential confounders was minimal (maximum, 3.0%). We imputed these data using multiple imputations by chained equations (5 data sets). We used a group-based trajectory modeling approach implemented by SAS Proc Traj and as described in the online supplemental material (expanded methods section, Tables S2-S4 and Figures S1-S2).[33] We identified five body silhouette trajectories based on the change in the Bayesian information criterion, and classified them based on their visual appearance, i.e. lean-stable, lean-increase,

lean-marked increase, moderate-stable and heavy-stable. We then calculated the posterior probability for each participant being a member of one of the five trajectories and assigned each participant into the trajectory to which their posterior probability was greatest. The average posterior probability for each trajectory ranged between 82%-90% indicating good allocation of individuals to the trajectories.[33] Trajectories were initially calculated stratified by sex, but trajectories were almost identical for men and women. Hence, the trajectories are described without stratification by sex.

We used multinomial logistic regression to evaluate associations between body silhouette trajectories and quartiles of carotid DC, YEM, IMT and diameter, and logistic regression to evaluate associations with resting hypertension and exaggerated exercise BP. We used the lean-stable group as the reference category in all analyses. We modeled carotid DC, YEM, IMT and diameter on a categorical scale, because such categorization provides results that are easier to interpret (odds ratios). We used ordinal regression analyses to test the proportional odds assumption, i.e. whether or not there is a graded association between body silhouette trajectories and manifestations of vascular aging. In addition, we used linear regression to evaluate the association between body trajectories and continuous values of carotid DC, YEM, IMT and diameter and resting and exercise systolic BP. We adjusted for the following potential confounders based on previous literature[10, 13-15, 34]: age, sex (only in analyses without sex-specific quartiles as the outcome), height, education, smoking, physical activity, dietary habits, heart rate, prior cardiovascular disease, diabetes, depressive symptoms and use of lipid-modifying medication. Analyses with carotid DC, YEM, IMT and diameter as the outcome were also adjusted for mean arterial pressure and use of antihypertensive medication.

We did several additional analyses: 1) we additionally adjusted the results for birth weight to test whether any of the tested associations could be explained by fetal growth; 2) to address residual confounding, we adjusted for cardiorespiratory fitness (as estimated by the validated NET-F algorithm[29]) instead of physical activity, and we adjusted for fasting glucose instead of diabetes; 3) to address possible reverse causality, we repeated the analyses after excluding individuals with prior cardiovascular disease; 4) we repeated the analyses after excluding individuals whose trajectory assignment probability was <80%; 5) we stratified the analyses by age categories (≤55 years, 55-65 years and >65 years) to evaluate whether associations were different according to the time difference between latest age of recalled body silhouette (45 years) and age at which vascular measurements were done; 6) we stratified the analyses by smoking behavior (never, current and former), because previous studies[23] have suggested that the association between body silhouette and mortality differs according to smoking status; 7) we stratified the analysis according to resting BP (<140/90 mmHg and ≥140/90 mmHg); 8) we additionally adjusted for current waist circumference or BMI to evaluate whether body silhouette trajectories may have any additional value in the association with vascular aging beyond measures of current adiposity; and 9) to evaluate the importance of increase of adiposity over the lifetime, we calculated the difference between the lean-marked increase trajectory on the one hand and the heavy-stable and moderate-stable trajectory on the other with regard to their association with manifestations of vascular aging.

## Results

### Body silhouette trajectories and study characteristics

We identified five distinct trajectories of body silhouette (Figure 2). Overall, 32.0% (n=2,641) of the participants maintained a lean body shape from age 8 until 45 (lean-stable group); 11.1% (n=917) started lean and then had a moderate increase in body shape (lean-increase); 32.5% (n=2,677) had a medium body shape and maintained weight (moderate-stable); 16.3% (n=1,340) started lean and then had a substantial gain of weight (lean-marked increase); and 8.1% (n=668) started heavy and maintained weight (heavy-stable). Characteristics of the total study population and according to body silhouette trajectory are shown in Table 1.

### Association with manifestations of vascular aging

Individuals in the trajectories moderate-stable, lean-marked increase and heavy-stable compared to those in the lean-stable trajectory had higher odds of having a lower carotid DC, higher YEM, higher IMT and higher diameter (Figure 3 and Table 2). In addition, individuals in the trajectories lean-increase, moderate-stable, lean-marked increase and heavy-stable compared to those in the lean-stable trajectory had higher odds of having resting hypertension and exaggerated exercise BP (Figure 3 and Table 2). The results of the ordinal regression analysis showed that the proportional assumption was met for all analyses, except for the analyses with carotid diameter as the outcome (supplemental material, Table S5). When carotid DC, YEM, IMT and diameter, and resting and exercise systolic BP were modeled as continuous variables, results were qualitatively similar (Table 3).

Additional analyses

Results did not materially change when we additionally adjusted for birth weight (Table S6) cardiorespiratory fitness (Table S7), fasting glucose (Table S8), or after excluding individuals with prior cardiovascular disease (n=171) (Table S9). In addition, when we repeated the analyses after excluding individuals whose trajectory assignment probability was <80% (n=2,209), effect estimates for the associations between body trajectories and manifestations of vascular aging became higher (Table S10). Furthermore, results were qualitatively similar in individuals aged ≤55, 55-65 and >65 years (Table S11), and in never, former and current smokers (Table S12). Body silhouette trajectories were associated with carotid DC, YEM, IMT and diameter, and exaggerated exercise BP irrespective of resting BP category (Table S13). Adjustments for current waist circumference (Table S14) or BMI (Table S15) attenuated the associations between body silhouette trajectories and manifestations of vascular aging. The attenuation was less for the lean marked-increase than for the heavy-stable trajectory. Some body silhouette trajectories, most often moderate-stable and lean-marked increase, remained statistically significantly associated with some manifestations of vascular aging. Finally, the lean-marked increase trajectory, as compared to the moderate-stable trajectory, had a statistically significantly higher odds of some manifestations of vascular aging (i.e. greater carotid IMT and diameter and exaggerated exercise BP) (Table S16). There were no differences between the lean-marked increase and heavy-stable trajectory (Table S16).

## Discussion

We evaluated the association between recalled body silhouettes over the lifespan and various manifestations of vascular aging in late adulthood. We found that participants who remained heavy from 8 to 45 years and even those who were lean in childhood but gained weight in young adulthood had the highest values of carotid stiffness, IMT and diameter, and highest odds of resting hypertension and exaggerated exercise BP, indicating evidence of advanced vascular aging. In contrast, those who maintained a stable-lean body silhouette had the lowest values of carotid stiffness, IMT and diameter, and lowest odds of resting hypertension and exaggerated exercise BP. These findings suggest that prevention of weight gain across the life course, in particular in young adulthood, is important to promote healthy vascular aging.

One previous study[16] retrospectively linked BMI measured in childhood and from an age of 36 to 60-64 years to carotid IMT and BP measured at an age of 60-64 years. This study found that in particular individuals that remained overweight from 36 to 60-64 years as compared to those without overweight during this time period had higher carotid IMT and systolic BP at an age of 60-64 years. We extend these results by investigating trajectories of adiposity across a wider age range and by investigating a larger number of manifestations of vascular aging. In our study, a marked increase in weight during young adulthood as compared to maintaining a lean weight was associated with a 0.9 kPa/$10^3$ lower carotid DC and 20 μm higher carotid IMT, which is equivalent to approximately 5 years of normal aging.[35, 36]

Some methodological issues warrant consideration. First, body silhouettes may represent an alternative to objectively and repeatedly measured adiposity manifestations across the life course in large observational studies when lifetime objective adiposity measures are not available.[26-28] However, some previous studies[21, 37] found a systematic bias in reporting of

body silhouettes: individuals with low BMI tended to overestimate their body size, whereas those with normal or high BMI tended to underestimate their body size. This may have led to an underestimation of the associations between body silhouette trajectories and manifestations of vascular aging. Confirmation of our results in a longitudinal study that prospectively evaluates adiposity over the life course would therefore be ideal. Second, we evaluated whether the associations between body trajectories and vascular aging were independent of BMI and waist circumference in late adulthood. However, these analyses should be interpreted with caution because adjustment for adiposity in late adulthood is likely to be an overadjustment, i.e. such adjustment controls not only for adult body size, but also for change in body weight across the life course. Furthermore, adulthood adiposity is likely to be on the causal path from childhood adiposity to accelerated vascular aging.[23] Nevertheless, these analyses showed that trajectories moderate-stable, lean-marked increase and heavy-stable remained statistically significantly associated with some manifestations of vascular aging. Furthermore, the attenuation was less for the lean marked-increase trajectory than for the heavy-stable trajectory. This may suggest that body trajectories can have additional predictive value beyond current objective measures of adiposity, in particular the lean-marked increase trajectory, but future prospective studies are needed to address this issue. Third, additional analyses suggested that increase in adiposity over the life time (i.e. lean-marked increase trajectory) may be at least as strongly associated with vascular aging as accumulation of high adiposity (i.e. moderate-stable and heavy-stable trajectories). However, these analyses should also be interpreted with caution, because of risk of false-positive findings due to multiple testing.

Several mechanisms may underlie the association between life course adiposity and vascular aging. Weight gain in young adulthood has been associated with sympathetic overactivity,

insulin resistance, low-grade inflammation, and lower adiponectin and higher leptin levels.[38] These factors may accelerate age-related fragmentation and depletion of elastin and deposition of collagen in the vascular media, thickening of the media layer, and compensatory arterial remodeling.[1] Ultimately, this may manifest as advanced vascular aging. In addition, body silhouette trajectories were associated with higher carotid stiffness, IMT and diameter and exaggerated exercise BP even in individuals with normal resting BP, suggesting that the effect of body adiposity on vascular aging is not only explained by increased resting BP. This is also in accordance with exaggerated exercise BP being associated with incident cardiovascular disease and mortality even among people with apparently controlled resting BP.[2]

Strengths of the present study include the detailed phenotypes of carotid artery properties in a large sample size with core-lab centralized reading. Furthermore, we were able to study various manifestations of vascular aging which enabled us to test the consistency of our associations.

The present study has several limitations. First, we did not have information about long-term lifestyle patterns including physical activity and dietary habits. These patterns may in part explain the observed findings. Second, the derived body silhouette trajectories are data driven, and may, therefore, vary by cohort. Third, birth weight was self-reported, which is less accurate than actual birth weight. Finally, no data were available on insulin resistance. Insulin resistance may partly explain the association between body silhouette trajectories and vascular aging.

In conclusion, a life course approach enables identification of body silhouette trajectories from age 8 up to 45 that are associated with vascular aging. Vascular aging was most prominent among individuals who were lean in early life but gained weight during young adulthood, and among those who were heavy in early life and maintained a heavy weight.

## Perspectives

The present study results suggest that healthy behaviors and environments to prevent weight gain across the life course, especially during young adulthood, are important to promote healthy vascular aging. Future studies should investigate determinants of lifetime trajectories of body silhouettes for development of strategies to promote healthy vascular aging.


## Sources of funding

PPS3 was supported by grants from The National Research Agency, the Research Foundation for Hypertension, the Research Institute in Public Health, and the Region Ile de France (Domaine d'Intérêt Majeur). RS is supported by a Prestige and Marie Curie Fellowship, a Lefoulon Delalande Fellowship, a High Blood Pressure Research Council of Australia Franco-Aus exchange grant and a L'Institute Servier grant. TVS is supported by a French National Research Agency grant.


## Conflict of interest

None.

References


1. Nilsson PM, Boutouyrie P, Cunha P, Kotsis V, Narkiewicz K, Parati G, Rietzschel E, Scuteri A, Laurent S. Early vascular ageing in translation: From laboratory investigations to clinical applications in cardiovascular prevention. *J Hypertens*. 2013;31:1517-1526
2. Schultz MG, Otahal P, Picone DS, Sharman JE. Clinical relevance of exaggerated exercise blood pressure. *J Am Coll Cardiol*. 2015;66:1843-1845
3. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: A meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet*. 2002;360:1903-1913
4. Lorenz MW, Markus HS, Bots ML, Rosvall M, Sitzer M. Prediction of clinical cardiovascular events with carotid intima-media thickness: A systematic review and meta-analysis. *Circulation*. 2007;115:459-467
5. van Sloten TT, Sedaghat S, Laurent S, London GM, Pannier B, Ikram MA, Kavousi M, Mattace-Raso F, Franco OH, Boutouyrie P, Stehouwer CDA. Carotid stiffness is associated with incident stroke: A systematic review and individual participant data meta-analysis. *J Am Coll Cardiol*. 2015;66:2116-2125
6. Olsen MH, Angell SY, Asma S, et al. A call to action and a lifecourse strategy to address the global burden of raised blood pressure on current and future generations: The lancet commission on hypertension. *Lancet*. 2016;388:2665-2712
7. Zachariah JP, Rong J, Larson MG, Hamburg NM, Benjamin EJ, Vasan RS, Mitchell GF. Metabolic predictors of change in vascular function: Prospective associations from a community-based cohort. *Hypertension*. 2018;71:237-242
8. Stevens J, Juhaeri, Cai J, Evans GW. Impact of body mass index on changes in common carotid artery wall thickness. *Obes Res*. 2002;10:1000-1007

9. Lee DH, Steffes MW, Gross M, Park K, Holvoet P, Kiefe CI, Lewis CE, Jacobs DR, Jr. Differential associations of weight dynamics with coronary artery calcium versus common carotid artery intima-media thickness: The cardia study. *Am J Epidemiol*. 2010;172:180-189

10. Jayedi A, Rashidy-Pour A, Khorshidi M, Shab-Bidar S. Body mass index, abdominal adiposity, weight gain and risk of developing hypertension: A systematic review and dose-response meta-analysis of more than 2.3 million participants. *Obes Rev*. 2018;19:654-667

11. Brunner EJ, Shipley MJ, Ahmadi-Abhari S, Tabak AG, McEniery CM, Wilkinson IB, Marmot MG, Singh-Manoux A, Kivimaki M. Adiposity, obesity, and arterial aging: Longitudinal study of aortic stiffness in the whitehall ii cohort. *Hypertension*. 2015;66:294-300

12. AlGhatrif M, Strait JB, Morrell CH, Canepa M, Wright J, Elango P, Scuteri A, Najjar SS, Ferrucci L, Lakatta EG. Longitudinal trajectories of arterial stiffness and the role of blood pressure: The baltimore longitudinal study of aging. *Hypertension*. 2013;62:934-941

13. Ferreira I, van de Laar RJ, Prins MH, Twisk JW, Stehouwer CD. Carotid stiffness in young adults: A life-course analysis of its early determinants: The amsterdam growth and health longitudinal study. *Hypertension*. 2012;59:54-61

14. Juonala M, Jarvisalo MJ, Maki-Torkko N, Kahonen M, Viikari JS, Raitakari OT. Risk factors identified in childhood and decreased carotid artery elasticity in adulthood: The cardiovascular risk in young finns study. *Circulation*. 2005;112:1486-1493

15. Juonala M, Magnussen CG, Berenson GS, Venn A, Burns TL, Sabin MA, Srinivasan SR, Daniels SR, Davis PH, Chen W, Sun C, Cheung M, Viikari JS, Dwyer T,

Raitakari OT. Childhood adiposity, adult adiposity, and cardiovascular risk factors. *N Engl J Med*. 2011;365:1876-1885

16. Charakida M, Khan T, Johnson W, Finer N, Woodside J, Whincup PH, Sattar N, Kuh D, Hardy R, Deanfield J. Lifelong patterns of bmi and cardiovascular phenotype in individuals aged 60-64 years in the 1946 british birth cohort study: An epidemiological study. *Lancet Diabetes Endocrinol*. 2014;2:648-654
17. Williamson DF, Kahn HS, Remington PL, Anda RF. The 10-year incidence of overweight and major weight gain in us adults. *Arch Intern Med*. 1990;150:665-672
18. Guo SS, Wu W, Chumlea WC, Roche AF. Predicting overweight and obesity in adulthood from body mass index values in childhood and adolescence. *Am J Clin Nutr*. 2002;76:653-658
19. Koprowski C, Coates RJ, Bernstein L. Ability of young women to recall past body size and age at menarche. *Obes Res*. 2001;9:478-485
20. Lonnebotn M, Svanes C, Igland J, et al. Body silhouettes as a tool to reflect obesity in the past. *PLoS One*. 2018;13:e0195697
21. Must A, Phillips SM, Naumova EN, Blum M, Harris S, Dawson-Hughes B, Rand WM. Recall of early menstrual history and menarcheal body size: After 30 years, how well do women remember? *Am J Epidemiol*. 2002;155:672-679
22. Must A, Willett WC, Dietz WH. Remote recall of childhood height, weight, and body build by elderly subjects. *Am J Epidemiol*. 1993;138:56-64
23. Song M, Hu FB, Wu K, Must A, Chan AT, Willett WC, Giovannucci EL. Trajectory of body shape in early and middle life and all cause and cause specific mortality: Results from two prospective us cohort studies. *BMJ*. 2016;353:i2195

24. Fagherazzi G, Vilier A, Affret A, Balkau B, Bonnet F, Clavel-Chapelon F. The association of body shape trajectories over the life course with type 2 diabetes risk in adulthood: A group-based modeling approach. *Ann Epidemiol*. 2015;25:785-787

25. Zheng Y, Song M, Manson JE, Giovannucci EL, Hu FB. Group-based trajectory of body shape from ages 5 to 55 years and cardiometabolic disease risk in 2 us cohorts. *Am J Epidemiol*. 2017;186:1246-1255

26. Empana JP, Bean K, Guibout C, Thomas F, Bingham A, Pannier B, Boutouyrie P, Jouven X, Group PPSS. Paris prospective study iii: A study of novel heart rate parameters, baroreflex sensitivity and risk of sudden death. *Eur J Epidemiol*. 2011;26:887-892

27. Stunkard AJ, Sorensen T, Schulsinger F. Use of the danish adoption register for the study of obesity and thinness. *Res Publ Assoc Res Nerv Ment Dis*. 1983;60:115-120

28. Proust C, Empana JP, Boutouyrie P, Alivon M, Challande P, Danchin N, Escriou G, Esslinger U, Laurent S, Li Z, Pannier B, Regnault V, Thomas F, Jouven X, Cambien F, Lacolley P. Contribution of rare and common genetic variants to plasma lipid levels and carotid stiffness and geometry: A substudy of the paris prospective study 3. *Circ Cardiovasc Genet*. 2015;8:628-636

29. Sharman JE, Boutouyrie P, Perier MC, Thomas F, Guibout C, Khettab H, Pannier B, Laurent S, Jouven X, Empana JP. Impaired baroreflex sensitivity, carotid stiffness, and exaggerated exercise blood pressure: A community-based analysis from the paris prospective study iii. *Eur Heart J*. 2018;39:599-606

30. Baecke JA, Burema J, Frijters JE. A short questionnaire for the measurement of habitual physical activity in epidemiological studies. *Am J Clin Nutr*. 1982;36:936-942

31. Oppert JM, Thomas F, Charles MA, Benetos A, Basdevant A, Simon C. Leisure-time and occupational physical activity in relation to cardiovascular risk factors and eating habits in french adults. *Public Health Nutr*. 2006;9:746-754

32. Pichot p. A self-report inventory on depressive symptomatology (qd2) and its abridged form (qd2). In assessment of depression. Springer. 1986:108-122.

33. Jones bl, nagin ds. Advances in group-based trajectory modeling and an sas procedure for estimating them. Sociol methods res. 2007;35(4):542-571.

34. Niiranen TJ, Lyass A, Larson MG, Hamburg NM, Benjamin EJ, Mitchell GF, Vasan RS. Prevalence, correlates, and prognosis of healthy vascular aging in a western community-dwelling cohort: The framingham heart study. *Hypertension*. 2017;70:267-274

35. Engelen L, Bossuyt J, Ferreira I, van Bortel LM, Reesink KD, Segers P, Stehouwer CD, Laurent S, Boutouyrie P, Reference Values for Arterial Measurements Collaboation. Reference values for local arterial stiffness. Part a: Carotid artery. *J Hypertens*. 2015;33:1981-1996

36. Engelen L, Ferreira I, Stehouwer CD, Boutouyrie P, Laurent S, Reference Values for Arterial Measurements Collaboration. Reference intervals for common carotid intima-media thickness measured with echotracking: Relation with risk factors. *Eur Heart J*. 2013;34:2368-2380

37. Tehard B, van Liere MJ, Com Nougue C, Clavel-Chapelon F. Anthropometric measurements and body silhouette of women: Validity and perception. *J Am Diet Assoc*. 2002;102:1779-1784

38. Hu F, ed. Obesity epidemiology. New york, ny: Oxford university press; 2008.

**Novelty and significance**

**1- What is new?**

- The association between adiposity over the life course and vascular aging in late adulthood is unknown.

**2- What is relevant?**

- Weight gain across the lifetime may be an important, modifiable determinant of vascular aging.

**3- Summary**

- We used a novel method to estimate adiposity trajectories across the life course using recalled body silhouettes from age 8 up to 45.
- Vascular aging was most prominent among individuals who were lean in early life but markedly gained weight during young adulthood, and among those who were heavy in early life and maintained weight.

**Figure Legends**

**Figure 1. Body silhouettes.** Body silhouettes for women and men in adults.

**Figure 2. Trajectories of body silhouettes.** Trajectories of body shape by age in women and men combined. Mean body shape levels on y-axis were estimated from trajectory models. Percentages represent the proportion of the study population in each trajectory.

**Figure 3**. **Associations between body silhouette trajectories and manifestations of vascular aging**: carotid distensibility coefficient (DC; quartile 1 vs. quartile 4); carotid Young's elastic modulus (YEM; quartile 4 vs. quartile 1); carotid intima-media thickness (IMT; quartile 4 vs. quartile 1); carotid diameter (quartile 4 vs. quartile 1); resting hypertension (blood pressure ≥140/90 mmHg or use of antihypertensive medication); and exaggerated exercise blood pressure (exercise BP; exercise systolic BP ≥150 mmHg). The lean-stable group served as the reference group in all analyses. Results are adjusted for age, sex (only in analyses without sex-specific quartiles as the outcome), height, education, smoking, physical activity, dietary habits, heart rate, prior cardiovascular disease, diabetes, depressive symptoms and use of lipid-modifying medication. Analyses with carotid DC, YEM, IMT and diameter as outcome were also adjusted for mean arterial pressure and use of antihypertensive medication. For cut-off values of sex-specific quartiles of carotid artery properties, see the online supplemental material.

**Table 1**. Characteristics for the total study population and according to body silhouette trajectory*

| Study population characteristics | Total study population | Body silhouette trajectory | | | | |
|---|---|---|---|---|---|---|
| | | Lean-stable | Lean-increase | Moderate-stable | Lean-marked increase | Heavy-stable |
| | n=8,243 | 32.0%; n=2,641 | 11.1%; n=917 | 32.5%; n=2,677 | 16.3%; n=1,340 | 8.1%; n=668 |
| *General characteristics* | | | | | | |
| Age (years) | 59.4 (6.2) | 59.4 (6.1) | 60.3 (6.4) | 59.3 (6.3) | 59.2 (6.3) | 58.8 (5.9) |
| Men | 61.3 (5,057) | 61.6 (1,626) | 71.5 (656) | 55.3 (1,481) | 74.0 (991) | 45.4 (303) |
| Education | | | | | | |
| Low | 27.7 (2,281) | 24.3 (643) | 28.2 (259) | 26.5 (710) | 34.1 (457) | 31.7 (212) |
| Middle | 30.2 (2,490) | 31.3 (827) | 27.5 (252) | 30.8 (825) | 29.4 (394) | 28.7 (192) |
| High | 41.2 (3,393) | 43.2 (1,140) | 43.0 (394) | 41.8 (1,119) | 36.0 (482) | 38.6 (258) |
| Smoking | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Current | 14.4 (1,190) | 13.4 (353) | 14.3 (131) | 15.6 (418) | 13.2 (177) | 16.6 (111) |
| Former | 33.8 (2,790) | 32.7 (863) | 35.8 (328) | 32.8 (877) | 37.9 (508) | 32.0 (214) |
| Never | 51.5 (4,247) | 53.9 (1,419) | 49.7 (456) | 51.5 (1,378) | 48.7 (653) | 51.0 (341) |
| Prior cardiovascular disease | 1.8 (151) | 1.3 (35) | 2.2 (20) | 2.0 (54) | 2.3 (31) | 1.6 (11) |
| Diabetes | 3.7 (302) | 2.0 (52) | 3.8 (35) | 3.4 (90) | 6.9 (93) | 4.8 (32) |
| Heart rate (bpm) | 62 (9) | 61 (9) | 61 (9) | 61 (9) | 63 (9) | 62 (9) |
| Body mass index ($kg/m^2$) | 25.1 (3.6) | 23.7 (3.0) | 24.1 (3.0) | 25.2 (3.4) | 26.7 (3.5) | 27.8 (4.5) |
| Physical activity (Baecke score) | 6.9 (1.6) | 6.9 (1.6) | 6.8 (1.6) | 6.9 (1.5) | 6.9 (1.6) | 6.8 (1.6) |
| Depressive symptoms | 11.8 (974) | 9.8 (258) | 10.5 (96) | 12.8 (342) | 12.6 (169) | 16.3 (109) |
| Antihypertensive medication | 14.7 (1,209) | 11.9 (315) | 16.0 (147) | 14.2 (381) | 19.0 (255) | 16.6 (111) |
| Lipid-modifying medication | 13.2 (1,089) | 10.9 (288) | 15.0 (138) | 12.4 (331) | 18.0 (241) | 13.6 (91) |
| *Manifestations of vascular aging* | | | | | | |
| Carotid Distensibility coefficient ($kPa^{-1}$ x $10^{-3}$) | 22.0 (8.0) | 22.6 (7.9) | 22.3 (8.3) | 21.8 (8.1) | 21.0 (7.7) | 21.7 (7.9) |
| Carotid Young's elastic modulus (kPa) | 4.93 (2.22) | 4.76 (2.06) | 4.92 (2.23) | 4.97 (2.28) | 5.19 (2.34) | 4.95 (2.24) |
| Carotid intima-media thickness (μm) | 638 (116) | 628 (112) | 641 (119) | 640 (116) | 650 (119) | 646 (115) |

| | | | | | | |
|---|---|---|---|---|---|---|
| Carotid diameter (mm) | 7.16 (0.71) | 7.10 (0.67) | 7.18 (0.70) | 7.13 (0.71) | 7.31 (0.71) | 7.16 (0.78) |
| Resting hypertension | 35.2 (2,904) | 29.5 (779) | 37.5 (344) | 35.8 (958) | 41.9 (562) | 39.1 (261) |
| Resting blood pressure | | | | | | |
| Systolic blood pressure (mmHg) | 131 (16) | 129 (16) | 132 (16) | 130 (16) | 133 (16) | 131 (16) |
| Diastolic blood pressure (mmHg) | 76 (10) | 75 (10) | 76 (10) | 75 (10) | 77 (10) | 76 (9) |
| Exaggerated exercise blood pressure | 44.8 (3,695) | 40.5 (1,069) | 45.0 (413) | 45.6 (1,221) | 50.4 (675) | 47.5 (317) |
| Exercise systolic blood pressure (mmHg) | 152 (19) | 150 (19) | 151 (19) | 152 (19) | 155 (19) | 154 (19) |

Data are means (SD) or % (n).

* Due to missing data, numbers or percentages for some variables do not sum to group totals or to 100%, respectively.

**Table 2.** Association between body silhouette trajectories and manifestations of vascular aging – results of intermediate quartiles

| Manifestations of vascular aging | Body silhouette trajectories | | | |
|---|---|---|---|---|
| | Lean-increase | Moderate-stable | Lean-marked increase | Heavy-stable |
| | Odds ratio (95% confidence interval) | | | |
| Distensibility coefficient | | | | |
| Q3 vs Q4 | 1.14 (0.91;1.42) | 1.25 (1.07;1.47) | 1.19 (0.98;1.43) | 1.22 (0.95;1.56) |
| Q2 vs Q4 | 1.17 (0.93;1.47) | 1.28 (1.09;1.51) | 1.32 (1.09;1.60) | 1.25 (0.97;1.61) |
| Q1 vs Q4 | 0.99 (0.79;1.25) | 1.39 (1.21;1.60) | 1.52 (1.23;1.87) | 1.50 (1.14;1.96) |
| Young's elastic modulus | | | | |
| Q2 vs Q1 | 1.13 (0.90;1.41) | 1.26 (1.08;1.48) | 1.17 (0.97;1.41) | 1.17 (0.92;1.50) |
| Q3 vs Q1 | 1.08 (0.86;1.36) | 1.24 (1.06;1.45) | 1.21 (1.00;1.47) | 1.15 (0.90;1.48) |
| Q4 vs Q1 | 0.91 (0.73;1.15) | 1.23 (1.06;1.44) | 1.27 (1.04;1.56) | 1.37 (1.05;1.78) |
| Intima-media thickness | | | | |
| Q2 vs Q1 | 1.01 (0.81;1.25) | 1.01 (0.87;1.17) | 1.15 (0.95;1.39) | 1.48 (1.16;1.89) |
| Q3 vs Q1 | 1.13 (0.90;1.41) | 1.12 (0.96;1.32) | 1.33 (1.10;1.69) | 1.32 (1.03;1.69) |
| Q4 vs Q1 | 1.00 (0.80;1.26) | 1.39 (1.17;1.64) | 1.67 (1.36;2.06) | 1.83 (1.41;2.37) |
| Diameter | | | | |
| Q2 vs Q1 | 1.05 (0.84;1.31) | 1.14 (0.97;1.33) | 1.32 (1.09;1.50) | 1.71 (1.36;2.19) |
| Q3 vs Q1 | 1.11 (0.88;1.39) | 1.17 (1.00;1.38) | 1.32 (1.09;1.61) | 1.63 (1.28;2.09) |
| Q4 vs Q1 | 0.86 (0.76;0.96) | 1.31 (1.11;1.54) | 1.71 (1.47;2.00) | 2.10 (1.62;2.72) |

Results adjusted for age, height, education, smoking, physical activity, dietary habits, heart rate, mean arterial pressure, use of antihypertensive medication, prior cardiovascular disease, diabetes, depressive symptoms and use of lipid-modifying medication. Lean-stable trajectory served as the reference in all analyses. For cut-off values of sex-specific quartiles, see the online supplemental material.

**Table 3.** Association between body silhouette trajectories and continuous measures of manifestations of vascular aging

| Trajectories | Distensibility coefficient ($kPa^{-1}*10^{-3}$) | Young's elastic modulus (kPa) | Intima-media thickness (μm) | Diameter (mm) | Resting systolic blood pressure (mmHg) | Exercise systolic blood pressure (mmHg) |
|---|---|---|---|---|---|---|
| | Regression coefficient (95% confidence interval) | | | | | |
| Lean-stable | Reference | | | | | |
| Lean-increase | 0.2 (-0.3;0.8) | 1 (-14;17) | 2 (-6;10) | -0.02 (-0.06;0.03) | 1 (0;3) | 0 (-1;2) |
| Moderate-stable | -0.6 (-1.9;-0.3) | 16 (5;27) | 13 (7;19) | 0.06 (0.03;0.10) | 1 (0;2) | 2 (1;4) |
| Lean-marked increase | -0.9 (-1.4;-0.4) | 22 (8;35) | 18 (11;25) | 0.14 (0.10;0.18) | 2 (1;3) | 3 (2;5) |
| Heavy-stable | -0.7 (-1.3;-0.1) | 12 (-6;30) | 23 (14;32) | 0.16 (0.10;0.21) | 2 (1;3) | 4 (3;6) |

Results are adjusted for age, sex, height, education, smoking, physical activity, dietary habits, heart rate, prior cardiovascular disease, diabetes, depressive symptoms and use of lipid-modifying medication. Analyses with carotid distensibility coefficient, Young's elastic modulus, intima-media thickness and diameter as outcome were also adjusted for mean arterial pressure and use of antihypertensive medication.