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Non-modifiable and Modifiable Risk Factors in Vascular Ageing Extremes: The African-PREDICT Study

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Abstract

Background Cardiovascular risk factors accelerate vascular ageing beyond chronological age, hence early vascular ageing (EVA). Carotid to femoral pulse wave velocity (cfPWV) is a measure of vascular ageing and is used to identify EVA and supernormal vascular ageing (SUPERNOVA). Vascular ageing is not completely understood in African populations. Therefore, we aimed to phenotype young South African adults stratified by cfPWV extremes in terms of non-modifiable and modifiable risk factors. This study included 1133 young adults (mean age: 24.5 years). We measured cfPWV using applanation tonometry. Body composition measures, self-reported 24-h dietary intake, smoking and alcohol consumption were included. Fasting blood samples were analysed for biochemical risk factors. Three groups based on cfPWV percentiles were compared and included SUPERNOVA (≤ 10th percentile), average vascular ageing (AVA, between 10 to 90th percentile) and EVA (≥ 90th percentile).

Results Chronological age, male sex, smoking, alcohol use, and blood pressure were incrementally higher across PWV groups (all p trend ≤ 0.007). Black ethnicity was higher ($p = 0.038$) in the SUPERNOVA group. In exploratory factor analysis, a factor pattern including mean arterial pressure and fasting glucose showed beneficial odds (OR 0.62, $p = 0.002$) for SUPERNOVA and higher likelihood (OR 2.10, $p < 0.001$) for EVA. Another factor pattern of socio-economic status and total dietary fat showed lower odds (OR 0.64, $p = 0.003$) for EVA.

Conclusion Poor lifestyle behavioural risk factors seem detrimental in the EVA group conferring a possible higher risk of future CVD.

Keywords Ageing, Pulse wave velocity, Risk factors, Risk stratification, Arterial stiffness

1 Background

Vascular ageing is the gradual change of the vascular structure and function which results in decreased arterial elasticity and increased arterial stiffening over the life course [1]. Non-modifiable and modifiable risk factors accelerate an individual's vascular age beyond the chronological age and causes a mismatch that is termed early vascular ageing (EVA) [2]. The extreme opposite of EVA also exists which manifests as the protection against accelerated biological ageing of arteries, a concept coined as super normal vascular ageing (SUPERNOVA) [2]. The vascular ageing process leads to arterial stiffening, a central element in the manifestation of cardiovascular disease (CVD) [3]. Therefore, it is unsurprising that adults with EVA reach subclinical and clinical manifestations of CVD earlier than the average population while SUPERNOVA individuals have preserved arterial wall elasticity

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during the life course despite being exposed to similar risk factors as EVA [2]. Carotid-femoral pulse wave velocity (cfPWV) is the current gold standard measure of structural central arterial ageing as it considers arterial wall stiffness, -thickness and -lumen area, which are all components that can be altered by the cumulative effects of adverse risk factors.[4–8] More recently, alterations in arterial wall stiffness, -thickness and -lumen area was demonstrated by dilated hypertrophic carotid phenotypes being linked to age-associated central arterial stiffening resulting in cfPWV increase through the life course [9]. Therefore, the normal distribution of cfPWV values of a study sample can be used to define EVA and SUPERNOVA using lower 10th and upper 90th percentiles [10].

The determinants of an adverse vascular ageing phenotype include non-modifiable risk factors such as older chronological age, sex, ethnicity, socioeconomic status (SES), or modifiable risk factors such as smoking, alcohol consumption, high saturated fat and sugar diet, and physical inactivity [2, 11]. Different cardiovascular risk scores have cemented the understanding that multiple risk factors are better predictors of cardiovascular events and that the risk factors have a cumulative effect throughout life [12–14]. Latest research has demonstrated that cumulative risk factors in young life contributes to an earlier risk for fatal and non-fatal CV events in adulthood [15]. Therefore, understanding the complete risk factor profile of a study sample may give more insight than investigating a single risk factor.

The effects of risk factors on vascular ageing are well-documented, especially in EVA but there is limited literature regarding SUPERNOVA and which factors are involved in arterial protection [2]. Furthermore, the exploration of vascular ageing extremes in young adults are scarce as most research focuses on middle-aged and older individuals [16–18]. Additionally, research pertaining to vascular ageing is scarce in an African context.[18–21] Therefore, we aimed to phenotype young South African adults based on vascular ageing extremes in terms of non-modifiable and modifiable risk factors. We also aimed to investigate the association of risk factors with cfPWV as an intermediate target organ damage measure.

2 Materials and Methods

2.1 Study Design and Setting

This study is part of the African Prospective study on the Early Detection and Identification of Cardiovascular Disease and Hypertension (African-PREDICT), for which the detailed methodology has been published elsewhere [22]. The African-PREDICT study is an ongoing study that initially recruited 1202 participants. Participants were invited from Potchefstroom and surrounding areas in the North West province of South Africa. The baseline recruitment for the African-PREDICT study took place from 2013 to 2017 and aimed to investigate the underpinning pathophysiological mechanisms involved in CVD as well as predictors of CVD in an apparently healthy, South African, young adult population. The baseline data of African-PREDICT is included in the current study. All procedures complied with the Declaration of Helsinki (2008) and conformed to the South Africa Medical Research Council guidelines of good clinical practice [23]. The privacy of participants was always taken into consideration and all measurements were done in private, temperature-controlled rooms. When all measurements were completed, the participants received transport back home.

2.2 Inclusion and Exclusion Criteria

The inclusion and exclusion criteria for the African-PREDICT have been published [22]. Briefly, the inclusion criteria were young (20–30 years), apparently healthy, Black and White men and women, with a normal screening office blood pressure (BP) (< 140/90 mmHg), who were not infected with a human immuno-deficiency virus, had no self-reported chronic disease (or treatment thereof) and were not pregnant or breastfeeding at the time of screening. In addition to the original exclusion criteria, this study excluded participants without cfPWV data or with data that did not meet the quality control standards ($N = 69$). The final number of participants included in the current study were 1133.

2.3 Questionnaires and General Demographics

Self-reported data were collected using a questionnaire. The data collected included age, sex, ethnicity, education, employment, and household income from which SES was calculated using a point system that was adapted from Kuppuswamy's Socioeconomic Status Scale for a South African environment [24]. The modified Kuppuswamy scale is commonly used to measure SES in urban and rural areas [24]. Lifestyle information such as smoking status and alcohol consumption were also self-reported. A 24-h dietary recall questionnaire was administered by a dietician. Macro- and micronutrient intake were calculated in the appropriate units using an algorithm developed by the Medical Research Council termed the South African Food Composition database [25]. The dietary variables of interest were total fat, saturated fat, total sugar and added sugar. The individual average intakes were calculated from three recorded days.

2.4 Anthropometric Measurements

2.4.1 Body Composition

All anthropometric measurements were performed according to guidelines as described by the International Society for the Advancement of Kinanthropometry [26]. Body height (m), determined by the SECA 213 Portable Stadiometer (SECA, Hamburg, Germany), and weight (kg) to the nearest 0.1 kg using the SECA 813 Electronic Scales (SECA, Hamburg, Germany) were measured. Waist (cm) circumference (WC) was measured three times (using the median) with a non-flexible tape measure to the nearest 0.1 cm (Lufkin Steel Anthropometric Tape; W606PM; Lufkin, Apex, USA). The body mass index (BMI) and waist-to-height ratio were calculated. Bioelectrical impedance measurements were performed to estimate body fat percentage (BF%) using a Bodystat 1500MDD dual-frequency analyser (Bodystat, Ltd, Ballakaap, UK). Bioelectrical impedance has been validated in the estimation of BF% compared with dual-energy X-ray absorptiometry [27].

2.5 Cardiovascular Measurements

2.5.1 Brachial Blood Pressure

Brachial BP measurements, further referred to as office BP, were performed using the Dinamap Procare 100 Vital Signs Monitor (GE Medical Systems, Milwaukee, USA) with appropriately sized GE Critikon latex-free DuraCuffs. Prior to the measurement being performed, participants were requested to fast from 10 pm the night before and were informed to only consume water and refrain from smoking, exercise, caffeine and alcohol. The participants were required to be in a seated resting state with the arm supported at heart level during the measurement. A set of two BP measurements were done on the left and on the right arms, with a five-minute interval between set one and set two. The mean of the four readings was used for all subsequent analyses. Office systolic blood pressure (SBP) and office diastolic blood pressure (DBP) were obtained, and office pulse pressure (PP) was calculated as office PP = mean office SBP − mean office DBP. Office mean arterial pressure (MAP) was further calculated as MAP = office diastolic BP + 0.412 (office PP) [28].

2.5.2 Pulse Wave Velocity

The SphygmoCor XCEL device (SphygmoCor XCEL, AtCor Medical Pty. Ltd., Sydney, Australia) was used to perform pulse wave analysis and then to measure cfPWV. The carotid-femoral pulse wave velocity measurement was performed as described by Laurent et al. [29] Pulse wave velocity was captured at the right carotid and femoral arterial pulse points. The participant remained in the supine position in a relaxed state during the time of the measurement. The measurement was performed twice and repeated if the two measurements differed by more than 0.5 m/s. The femoral artery wave form was captured via an appropriately sized cuff placed around the right thigh, and the right carotid arterial waveform was captured simultaneously via applanation tonometry. The distances between the pulsated sites (carotid and femoral) were measured and the travel distance was calculated as 80% of the distance measured between the carotid pulse point and femoral cuff [30].

2.6 Blood Sampling and Biochemical Analysis

Blood collection was performed by a qualified nurse. Blood samples were aliquoted and stored in bio-freezers at − 80 °C. Serum analyses included the lipid profile (total cholesterol, low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL)), high-sensitivity CRP, and γ-glutamyl transferase (GGT) (Cobas Integra 400plus, Roche, Basel, Switzerland). Sodium fluoride plasma glucose was also determined on the turbidimetric inhibition immunoassay (TINIA) for homolysed whole blood (Cobas Integra 400 plus, Roche, Basel, Switzerland). Reactive oxygen species was measured as serum peroxides (reported as units, where 1 mg H_2O_2/L is equivalent to one unit) using a high throughput spectrophotometric assay and analysed on a Synergy HT microplate reader (BioTek, Winooski, VT, USA). The antioxidant marker superoxide dismutase was measured using assay kits (Randox, Co. Antrim, Ireland, UK) and the automated Cobas Integra 400 plus (Roche). A MILLIPEX Map Human High Sensitivity T Cell Magnetic Bead Panel (EMD Millipore, Merck, Missouri, USA) was used to analyse interleukin-6 from baseline samples, using Luminex xMAP technology on the Luminex 200™ analyser [31].

2.7 Statistical Analysis

The participants were categorised into three groups based on the 10th (SUPERNOVA, $n = 113$), 10th–90th (AVA, $n = 901$), and 90th (EVA, $n = 119$) percentiles of cfPWV. Statistical analyses were performed with IBM® SPSS® Statistics version 29 software (IBM Corporation; Armonk, New York, USA). Continuous variables were evaluated for normality by visual inspection (*QQ* plots) and variables that were not normally distributed were log-transformed. Normally distributed variables were presented as arithmetic mean ± standard deviation, non-Gaussian variables as geometric mean with 95th confidence interval and categorical data as proportions.

Analysis of covariance (ANCOVA) was performed to compare modifiable- and non-modifiable risk factors between the three groups while adjusting for sex

and ethnicity. To identify patterns of risk factors, a factor analysis was performed using the factor function of principal component analysis where factors with an eigenvalue of > 1 were retained. The Oblimin rotation with Kaizer normalization was used to obtain the independent interpretable factors [32]. Variables with a factor loading of ≥ 0.5 were retained in the factor patterns. Factor scores with a cumulative percentage of > 50% was used for logistic regression analyses. Logistic regression models were performed and were adjusted for sex and ethnicity and displayed as a forest plot. The AVA group was used as reference for comparison.

An a priori power analysis was performed to compute the required sample size using G*Power v3.1.9.2 software [33]. The preselected power was 95% at a significance level of $\alpha = 0.05$ and a medium effect size of $d = 0.5$ for arterial stiffness as the main outcome measure. The analysis calculated that an N-value (sample) of at least 105 per group is needed. Our sample sizes of $N = 119$ in the EVA group and $N = 113$ in the SUPERNOVA group would be sufficient to test the hypotheses of this study.

3 Results

Table 1 represents the characteristics of the study population stratified by PWV categories. In terms of demographics, the EVA group was older ($p < 0.001$) and consisted of more men ($p < 0.001$) but the absolute difference in age was small compared to the SUPERNOVA group. Black ethnicity was higher ($p = 0.038$) in the SUPERNOVA group. Alcohol use ($p = 0.007$) and smoking ($p < 0.001$) were more frequent in the EVA group. Blood pressure measures (office SBP and—DBP, and—MAP) were overall higher ($p < 0.001$) in the EVA group than in the SUPERNOVA group. No differences between vascular ageing groups with dietary factors and biochemical markers was present.

The results of the exploratory factor analysis performed in the total study sample are contained in Table 2. Three-factor patterns were identified, with the first factor consisting of BF%, BMI, REE, and CRP (Factor 1). The second factor was comprised of MAP and glucose (Factor 2), while the third factor included SES and total dietary fat (Factor 3).

In both SUPERNOVA and EVA models, factor 1 was not significant in terms of the odds of being in any vascular ageing group as demonstrated by Fig. 1. Factor 2 showed a 31% lower likelihood of higher MAP and fasting glucose (OR 0.62, $p = 0.002$) contributing to SUPERNOVA and higher odds (OR 2.10, $p < 0.001$) for EVA. Factor 3 showed a 36% lower likelihood of SES and total dietary fat (OR 0.64, $p = 0.003$) contributing to (EVA).

4 Discussion

In this study of young South African adults stratified by cfPWV percentiles, the EVA group had a less favourable phenotype of non-modifiable (older age and male sex) and modifiable risk factors (higher alcohol consumption and smoking and BP measures) when compared to the SUPERNOVA group. On the other hand, more black individuals were in the SUPERNOVA group. Furthermore, factor 2 showed a 38% lower likelihood of higher MAP and fasting glucose being in the SUPERNOVA group and 110% higher odds for EVA. Factor 3 showed a 36% lower likelihood of SES and total dietary fat being in EVA participants.

Our observation in the EVA group with regards to the non-modifiable risk factors are in line with previous findings showing an age- and sex- associated increase in cfPWV [34, 35]. It is well known that compliance decreases with age.[35] This age-associated vascular remodelling process is due to decreased elastin and increased collagen, reducing arterial distensibility [35]. The EVA group had a higher percentage of men and it is known that in premenopausal women, endogenous oestrogen levels, the number of arterial oestrogen receptors, and nitric-oxide (NO) production are higher and the beneficial effects may underlie the protection of premenopausal women against accelerated vascular ageing [34]. The EVA group had a more adverse profile in terms of the modifiable risk factors which included self-reported smoking and alcohol consumption, both known to promote endothelial dysfunction which may accelerate vascular ageing [36, 37]. This adverse risk factor profile in our healthy sample may point towards possible earlier manifestation of CVD events if the lifestyle behaviours remain unchanged [2].

Overall group differences in ethnicity were absent, as previously reported, but comparing the extreme 10th and 90th percentiles gave a borderline significant result of more black individuals in the SUPERNOVA group [38]. On the contrary, research findings demonstrate a clear trend that young adult (< 30 years) black populations had higher cfPWV than other ethnicities [39, 40]. The above-mentioned beneficial effects of premenopausal women may be at play as most of the participants in the SUPERNOVA group are women [34]. Further research may elucidate whether sex dimorphic differences in young adults are better predictors of vascular age than ethnic differences. Black participants have been noted to have a pronounced increase in cfPWV with ageing than white men and women [41]. Therefore, while the current healthy vascular age group has more black participants it is yet to be seen if this is the case at 5-year follow-up.

Using principal component analysis, a 38% lower likelihood of higher MAP and fasting glucose being in

Table 1 Comparisons of non-modifiable-, modifiable risk factors, cardiovascular measures, and biochemical markers between vascular ageing groups adjusted for sex and ethnicity

	SN (cfPWV ≤ 5.32 m/s)	AVA (middle)	EVA (cfPWV ≥ 7.52 m/s)	*p*-values			
	N = 113	*N* = 901	*N* = 119	Overall	SN vs AVA	SN vs EVA	AVA vs EVA
Demographics							
Age (years)	23.4 ± 2.98	24.5 ± 3.11	25.8 ± 2.79	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p < 0.001$
Sex (male)	10/113 (8.8)	444/901 (49.3)	97/119 (81.5)	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p < 0.001$
Ethnicity (Black)	60/113 (53.1)	458/901 (50.8)	47/119 (39.5)	$p = 0.050$	NS	$p = 0.038$	$p = 0.020$
Socio economic status (score)	20.0 ± 5.82	20.6 ± 6.06	21.6 ± 6.28	NS	NS	NS	NS
Lifestyle							
Smokers (at least once a week)	8/113 (7.1)	220/900 (24.4)	43/119 (36.1)	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p = 0.006$
Alcohol (at least once a week)	53/113 (46.9)	499/895 (55.8)	76/118 (64.4)	$p = 0.028$	NS	$p = 0.007$	NS
Body composition							
Body height (m)	1.67 ± 0.06	1.69 ± 0.06	1.71 ± 0.06	$p < 0.001$	$p = 0.039$	$p < 0.001$	$p < 0.001$
Body weight (kg)	69.4 ± 15.2	70.2 ± 14.7	70.8 ± 15.1	NS	NS	NS	NS
Waist circumference (cm)	79.1 ± 11.5	79.4 ± 11.1	79.9 ± 11.4	NS	NS	NS	NS
Body mass index (kg/m^2)	24.4 (23.6; 25.3)	24.2 (23.9;24.5)	23.7 (22.9; 24.5)	NS	NS	NS	NS
Body fat percentage (%)	24.5 ± 7.22	24.4 ± 7.0	23.4 ± 7.17	NS	NS	NS	NS
Waist-to-height ratio (ratio)	0.47 (0.46; 0.48)	0.47 (0.46; 0.47)	0.46 (0.45; 0.47)	NS	NS	NS	NS
Cardiovascular measures							
Office SBP (mmHg)	114 ± 10.6	118 ± 30.0	124 ± 10.9	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p < 0.001$
Office DBP (mmHg)	73.4 ± 7.15	78.2 ± 6.91	85.3 ± 7.10	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p < 0.001$
Office MAP (mmHg)	89.9 ± 7.80	94.3 ± 7.53	101 ± 7.74	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p < 0.001$
Office heart rate (bpm)	62.0 ± 9.45	64.1 ± 9.13	65.4 ± 9.38	$p = 0.028$	NS	$p = 0.027$	NS
Dietary intake							
Total dietary fat (g)	74.3 ± 10.4	74.1 ± 29.6	73.7 ± 10.8	NS	NS	NS	NS
Saturated fat (g)	20.0 (18.0; 22.4)	20.0 (19.3; 20.8)	20.5 (18.4; 22.7)	NS	NS	NS	NS
Total sugar (g)	40.6 (33.8; 48.8)	42.0 (39.5; 44.7)	49.1 (41.2; 58.5)	NS	NS	NS	NS
Biochemical markers							
Glucose (mg/dL)	89.9 (88.5; 91.2)	90.5 (90.1; 91.0)	91.2 (89.9; 92.6)	NS	NS	NS	NS
Gamma-glutamyl transferase (U/L)[1]	17.0 (15.1; 19.1)	17.7 (17.0; 18.4)	20.8 (18.6; 23.4)	$p = 0.021$	NS	NS	$p = 0.023$
HDL (mg/dL)	20.9 (19.5; 22.3)	19.1 (18.7; 19.6)	21.1 (19.8; 22.5)	$p = 0.002$	NS	NS	$p = 0.019$
LDL (mg/dL)	41.4 (38.4; 44.9)	40.2 (39.1; 41.3)	39.1 (36.4; 42.2)	NS	NS	NS	NS
Total cholesterol (mg/dL)	65.8 (61.8; 69.9)	63.4 (62.2; 64.9)	64.9 (61.1; 68.8)	NS	NS	NS	NS
Triglycerides (mg/dL)	11.9 (10.8; 13.2)	13.0 (12.6; 13.5)	13.0 (11.9; 14.4)	NS	NS	NS	NS
Total cholesterol to HDL (ratio)	3.15 (2.97; 3.33)	3.32 (3.25; 3.38)	3.08 (2.91; 3.25)	$p = 0.012$	NS	NS	$p = 0.035$
Triglycerides to HDL (ratio)	0.57 (0.51; 0.64)	0.68 (0.65; 0.70)	0.62 (0.56; 0.69)	$p = 0.006$	$p = 0.011$	NS	NS
C-reactive protein (mg/L)*	0.81 (0.62; 1.07)	0.85 (0.77; 0.93)	0.77 (0.60; 1.00)	NS	NS	NS	NS
Reactive oxygen species (mmol/L)	36.6 (32.5; 41.2)	37.9 (36.4; 39.5)	43.2 (38.5; 48.4)	NS	NS	NS	NS
Interleukin-6 (pg/mL)	1.06 (0.93; 1.20)	1.05 (1.00; 1.10)	0.99 (0.88; 1.12)	NS	NS	NS	NS
Tumour-necrosis factor alpha (pg/mL)	1.03 (0.93; 1.15)	1.05 (1.02; 1.09)	1.07 (0.97; 1.19)	NS	NS	NS	NS
Superoxide dismutase (U/mL)	4.26 (3.88; 4.66)	4.07 (3.94; 4.20)	3.93 (3.60; 4.30)	NS	NS	NS	NS

Pulse wave velocity groups were stratified as: SUPERNOVA (≤ 10th percentile) and EVA (≥ 90th percentile). Proportions are calculated with chi-square and reported as sample (percent within pulse wave velocity group). Data are reported as mean and standard deviation or geometric mean and 95% confidence interval

SN super normal vascular aging; *AVA* average vascular aging; *EVA* early vascular aging, *office SBP* office systolic blood pressure, *office DBP* office diastolic blood pressure, *office MAP* office mean arterial pressure, *HDL* high-density lipoprotein cholesterol, *LDL* low-density lipoprotein cholesterol, *NS* not significant

[1] GGT adjusted for sex, ethnicity, and alcohol use (at least once a week)

*C-reactive protein reported as median and (IQR)

Table 2 Factors identified in the total sample of young adults

	Factor 1	Factor 2	Factor 3
Body fat percentage (%)	0.876		
Body mass index (kg/m^2)	0.829		
Resting energy expenditure (kCal/day/kg)	-0.0827		
C-reactive protein (mg/L)	0.695		
Mean arterial pressure (mmHg)		0.847	
Glucose (mg/dL)		0.678	
Socio-economic status (score)			-0.790
Total dietary fat (g)			-0.738

Extraction method: principal component analysis. Rotation method: Oblimin rotation with Kaizer Normalization

SUPERNOVA was confirmed. Mean arterial pressure is a main determinant of cfPWV and it is known that the incidence of type-2 diabetes increases as the population ages and this change is due to the age-associated beta-cell function and insulin sensitivity [42]. Indeed, chronically elevated blood glucose and the consequence of advanced glycosylation end products (AGE) may be at play during arterial ageing [42]. The AGE products are key in an important mechanism in arterial stiffening, which leads to the cross-linking of collagen in arterial wall resulting in advanced vascular age [42, 43]. However, the SUPERNOVA group overall having lower levels of the risk factors, in conjunction with factor 2 having a lower likelihood, can explain such a beneficial finding in the SUPERNOVA group. A 110% higher likelihood of higher MAP and fasting glucose being in EVA was found. Individuals with elevated glucose levels usually have higher BP and advanced vascular age (arterial stiffness) [44, 45]. Indeed, diabetes is associated with not only hypertension but also arterial stiffness [46]. Therefore, monitoring fasting glucose levels in clinical practice may thus play a role in informing the advancement of vascular ageing as fasting glucose had a higher likelihood for vascular ageing because even in our young healthy individuals with glucose in normal ranges, fasting glucose formed part of this identified factor.

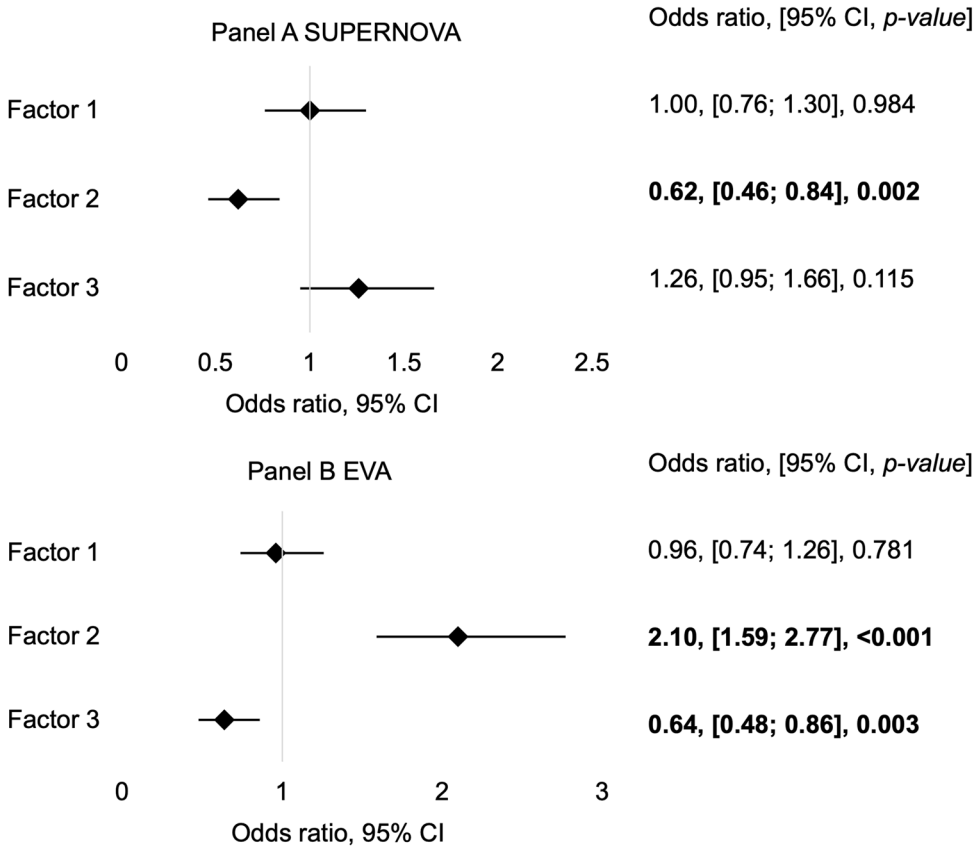

Fig. 1 Odds of principal component factors being present in vascular ageing groups. Adjusted for sex and ethnicity. Bold text indicates significance. *SUPERNOVA* super normal vascular ageing, *EVA* early vascular ageing

Factor 3 showed a 36% lower likelihood of SES and total dietary fat contributing to EVA. The reported likelihood denotes the absence of the effect of the components in the factor on advancing vascular ageing in the current population. Socio-economic status amplifies worsening vascular outcomes and its lower likelihood may point to other factors playing a bigger role in advancing vascular ageing in the current population [47]. Higher dietary fat contributes to arterial ageing by the effects of lipid metabolism and the atherogenic effect thereof on the arterial wall [48]. However, it forms part of the current factor with lower odds, therefore supporting that these young adults have a healthy cardiometabolic profile and that possible negative contributions to vascular ageing are not visible yet.

In closing, despite the noted adverse risk factor profile in EVA, our participants were CVD-free, and levels of the biochemical markers and cardiovascular measures were within normal ranges. Therefore, even at normal levels in a population free from CVD, we already see differences in vascular ageing based on risk factor phenotype. These findings show a potential early onset link of risk factors with PWV as an intermediate target organ damage marker. The possible implications of our findings point towards an adverse phenotype causing an abnormal rate of arterial ageing and such individuals being at earlier risk for CVD. Early clinical intervention would curb such possible future cardiovascular events [10]. This is relevant as recent findings have confirmed that lifestyle modification reduces absolute CVD risk score in adult populations without CVD [49].

5 Strengths and Limitations

The exploration of these extremes in young adults is scarce especially in an African context and the current study is the first study in young adults in South Africa to investigate vascular ageing extremes. The known limitation of cross-sectional studies and its inability to confirm causality applies and the findings may not be representative of the entire South African population as the participants are from a specific location within the North-West Province.

6 Conclusion

Poor lifestyle behaviour-related risk factors seem detrimental in the EVA group conferring a possible higher risk of future CVD. Furthermore, in the young adult South African population composite factors associated with PWV show a possible early onset link with this intermediate target organ damage marker.

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Author contributions
DR collected, analysed, and interpreted cfPWV data from participants in the African-PREDICT study. DR also drafted the manuscript. YB, RK, and EJvR were part of the conception, design, and interpretation of the data. They substantively revised the work. All authors read and approved the final manuscript and take accountability for the integrity and accuracy of their contributions.

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Availability of data and materials
The dataset analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest
The authors declare that they have no competing interests.

Ethics approval and consent to participate
The larger African-PREDICT (NWU-00001-12-A1) study and the current substudy (NWU-00022-23-S1) were approved by the North-West University Health Research Ethics Committee. Written informed consent was obtained from prospective participants to participate in the screening and research measurement stages, and participants were included if they satisfied the inclusion criteria.

Consent for publication
Not applicable.

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References

1. Laina A, Stellos K, Stamatelopoulos K. Vascular ageing: underlying mechanisms and clinical implications. Exp Gerontol. 2018;109:16–30.
2. Laurent S, Boutouyrie P, Cunha PG, Lacolley P, Nilsson PM. Concept of extremes in vascular aging. Hypertension. 2019;74(2):218–28.
3. Ungvari Z, Tarantini S, Donato AJ, Galvan V, Csiszar A. Mechanisms of vascular aging. Circ Res. 2018;123(7):849–67.
4. Mancia G, Kreutz R, Brunström M, Burnier M, Grassi G, Januszewicz A, et al. 2023 ESH Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension: Endorsed by the International Society of Hypertension (ISH) and the European Renal Association (ERA). J Hypertens. 2023;41(12):1874–2071.
5. Karikkineth A, AlGhatrif M, Oberdier M, Morrell C, Palchamy E, Strait J, et al. Sex differences in longitudinal determinants of carotid intima medial thickening with aging in a community-dwelling population: The Baltimore Longitudinal Study On Aging. J Am Heart Assoc. 2020;9(22):e015396.
6. Gerstenblith G, Frederiksen J, Yin FC, Fortuin NJ, Lakatta EG, Weisfeldt ML. Echocardiographic assessment of a normal adult aging population. Circulation. 1977;56(2):273–8.

7. AlGhatrif M, Strait JB, Morrell CH, Canepa M, Wright J, Elango P, et al. Longitudinal trajectories of arterial stiffness and the role of blood pressure: the Baltimore Longitudinal Study of Aging. Hypertension. 2013;62(5):934–41.
8. Oberdier MT, Morrell CH, Lakatta EG, Ferrucci L, AlGhatrif M. Subclinical longitudinal change in ankle-brachial index with aging in a community-dwelling population is associated with central arterial stiffening. J Am Heart Assoc. 2019;8(15): e011650.
9. AlGhatrif M, Lakatta EG, Morrell CH, Fegatelli DA, Fiorillo E, Marongiu M, et al. Dilated hypertrophic phenotype of the carotid artery is associated with accelerated age-associated central arterial stiffening. Geroscience. 2023;45(2):1001–13.
10. Cunha PG, Boutouyrie P, Nilsson PM, Laurent S. Early vascular ageing (EVA): definitions and clinical applicability. Curr Hypertens Rev. 2017;13(1):8–15.
11. Hall WL. Dietary saturated and unsaturated fats as determinants of blood pressure and vascular function. Nutr Res Rev. 2009;22(1):18–38.
12. Bosomworth NJ. Practical use of the Framingham risk score in primary prevention: Canadian perspective. Can Fam Physician. 2011;57(4):417–23.
13. Wong ND, Budoff MJ, Ferdinand K, Graham IM, Michos ED, Reddy T, et al. Atherosclerotic cardiovascular disease risk assessment: an American Society for Preventive Cardiology clinical practice statement. Am J Prev Cardiol. 2022;10: 100335.
14. Halcox JP, Tubach F, Sazova O, Sweet S, Medina J. Reclassification of European patients' cardiovascular risk using the updated Systematic Coronary Risk Evaluation algorithm. Eur J Prev Cardiol. 2015;22(2):200–2.
15. Jacobs DR Jr, Woo JG, Sinaiko AR, Daniels SR, Ikonen J, Juonala M, et al. Childhood cardiovascular risk factors and adult cardiovascular events. N Engl J Med. 2022;386(20):1877–88.
16. Niiranen TJ, Lyass A, Larson MG, Hamburg NM, Benjamin EJ, Mitchell GF, et al. Prevalence, correlates, and prognosis of healthy vascular aging in a western community-dwelling cohort: the framingham heart study. Hypertension. 2017;70(2):267–74.
17. Bruno RM, Nilsson P, Ensgrtom G, Wadstrom B, Empana J-P, Boutouyrie P, et al. 1.2 chronological versus vascular age: predictive value for cardiovascular events and identification of patients with SUPERNOrmal Vascular Aging (SUPERNOVA). Artery Res. 2019;25(1):S2.
18. Gomez-Sanchez M, Gomez-Sanchez L, Patino-Alonso MC, Cunha PG, Recio-Rodriguez JI, Alonso-Dominguez R, et al. Vascular aging and its relationship with lifestyles and other risk factors in the general Spanish population: Early Vascular Ageing Study. J Hypertens. 2020;38(6):1110–22.
19. Tao B, Li Y, Wang C, Luo X, Chen S, Wang G, et al. Influencing factors of supernormal vascular aging in Chinese population. J Hypertens. 2022;40(2):381–8.
20. Pereira T, Paulino E, Rosa M, Pinto A, Teixeira M, Soares P, et al. Study on the prevalence and determinants of early vascular ageing in a community setting—preliminary results from the asinphar@2action project. J Hypertens. 2018;36(1): e199.
21. Botto F, Obregon S, Rubinstein F, Scuteri A, Nilsson PM, Kotliar C. Frequency of early vascular aging and associated risk factors among an adult population in Latin America: the OPTIMO study. J Hum Hypertens. 2018;32(3):219–27.
22. Schutte AE, Gona PN, Delles C, Uys AS, Burger A, Mels CM, et al. The African Prospective study on the Early Detection and Identification of Cardiovascular disease and Hypertension (African-PREDICT): design, recruitment and initial examination. Eur J Prev Cardiol. 2019;26(5):458–70.
23. World Medical A. World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. Bulletin of the World Health Organization. 2001;79(4):373–4.
24. Patro BK, Jeyashree K, Gupta PK. Kuppuswamy's socioeconomic status scale 2010-the need for periodic revision. Indian J Pediatr. 2012;79(3):395–6.
25. Wolmarans P, Danster N, Dalton A, SAMRC. Condensed food composition tables for South Africa. Cape Town, South Africa: Medical Research Council; 2010.
26. Stewart A, Marfell-Jones M, Olds T, De Ridder J. International standards for anthropometric assessment. Wellington: International Society for the Advancement of Kinanthropometry; 2011.
27. Shafer K, Siders W, Johnson L, Lukaski H. Validity of segmental multiple-frequency bioelectrical impedance analysis to estimate body composition of adults across a range of body mass indexes. Nutrition. 2009;25(1):25–32.
28. Meaney E, Alva F, Moguel R, Meaney A, Alva J, Webel R. Formula and nomogram for the sphygmomanometric calculation of the mean arterial pressure. Heart. 2000;84(1):64.
29. Laurent S, Cockcroft J, Van Bortel L, Boutouyrie P, Giannattasio C, Hayoz D, et al. Expert consensus document on arterial stiffness: methodological issues and clinical applications. Eur Heart J. 2006;27(21):2588–605.
30. Van Bortel LM, Laurent S, Boutouyrie P, Chowienczyk P, Cruickshank JK, De Backer T, et al. Expert consensus document on the measurement of aortic stiffness in daily practice using carotid-femoral pulse wave velocity. J Hypertens. 2012;30(3):445–8.
31. Crouch SH, Roux SB, Delles C, Graham LA, Schutte AE. Distinct inflammatory mediator patterns in young black and white adults: The African-predict study. Cytokine. 2020;126: 154894.
32. Jackson JE. Oblimin rotation. Encyclopedia of biostatistics; 2005.
33. Faul F, Erdfelder E, Buchner A, Lang A. Statistical power analyses using G* Power 3.1: tests for correlation and regression analyses. Behav Res Methods. 2009;41(4):1149–60.
34. Ogola B, Zimmerman M, Clark G, Abshire C, Gentry K, Miller K, et al. New insights into arterial stiffening: does sex matter? Am J Physiol Heart Circ Physiol. 2018;315(5):H1073–87.
35. Kucharska-Newton AM, Stoner L, Meyer ML. Determinants of vascular age: an epidemiological perspective. Clin Chem. 2019;65(1):108–18.
36. Mahmud A, Feely J. Effect of smoking on arterial stiffness and pulse pressure amplification. Hypertension. 2003;41(1):183–7.
37. Kudo R, Yuui K, Hatake K. Alcohol and pathophysiology. In: Ishikawa T, editor. Forensic medicine and human cell research: new perspective and bioethics. Singapore: Springer Singapore; 2019. p. 45–64.
38. Breet Y, Huisman HW, Kruger R, van Rooyen J, Gafane-Matemane L, Ware L, et al. Pulse pressure amplification and its relationship with age in young, apparently healthy black and white adults: The African-PREDICT study. Int J Cardiol. 2017;2017(249):387–91.
39. Liang X, Su S, Hao G, Snieder H, Treiber F, Kapuku G, et al. Determinants of pulse wave velocity trajectories from youth to young adulthood: the Georgia Stress and Heart Study. J Hypertens. 2019;37(3):563–71.
40. Cruickshank J, Silva M, Molaodi O, Enayat Z, Cassidy A, Karamanos A, et al. Ethnic differences in and childhood influences on early adult pulse wave velocity: The determinants of adolescent, now young adult, social wellbeing, and health longitudinal study. Hypertension. 2016;67(6):1133–41.
41. Schutte AE, Kruger R, Gafane-Matemane LF, Breet Y, Strauss-Kruger M, Cruickshank JK. Ethnicity and arterial stiffness. Arterioscler Thromb Vasc Biol. 2020;40(5):1044–54.
42. Nilsson PM. Early vascular aging (EVA): consequences and prevention. Vasc Health Risk Manag. 2008;4(3):547–52.
43. Aronson D. Cross-linking of glycated collagen in the pathogenesis of arterial and myocardial stiffening of aging and diabetes. J Hypertens. 2003;21(1):3–12.
44. Franklin SS. Do diabetes and hypertension interact to accelerate vascular ageing? J Hypertens. 2002;20(9):1693–6.
45. Goldin A, Beckman JA, Schmidt AM, Creager MA. Advanced glycation end products: sparking the development of diabetic vascular injury. Circulation. 2006;114(6):597–605.
46. Tian X, Zuo Y, Chen S, Zhang Y, Zhang X, Xu Q, et al. Hypertension, arterial stiffness, and diabetes: a prospective cohort study. Hypertension. 2022;79(7):1487–96.
47. Puolakka E, Pahkala K, Laitinen T, Magnussen C, Hutri-Kähönen N, Kähönen M, et al. Childhood socioeconomic status and arterial stiffness in adulthood. Hypertension. 2017;70(4):729–35.
48. Millen BE, Quatromoni PA, Nam BH, O'Horo CE, Polak JF, D'Agostino RB. Dietary patterns and the odds of carotid atherosclerosis in women: the Framingham Nutrition Studies. Prev Med. 2002;35(6):540–7.
49. Kariuki JK, Imes CC, Engberg SJ, Scott PW, Klem ML, Cortes Y. Impact of lifestyle-based interventions on absolute cardiovascular disease risk: a systematic review and meta-analysis. JBI Evid Synth. 2024;22(1):4–65.