Low BMI is inversely associated with arterial stiffness in Africans

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Abstract

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In low socio-economic status communities in South Africa, African men showed a low BMI. Data on the effect of low BMI on cardiovascular function are scant. The present study aimed to assess the associations between low BMI and markers of cardiovascular function such as pulse wave velocity (PWV) and blood pressure in Africans aged 35–65 years, with low socio-economic status. The study population (*n* 496) was stratified into a low-BMI group with BMI $\leq 20 \text{ kg/m}^2$ and a normal-BMI group with BMI $> 20 \text{ kg/m}^2$ and $\leq 25 \text{ kg/m}^2$. Blood pressure (Omron HEM-757) and PWV (Complior SP; Artech-Medical) was determined. Africans with low BMI showed an increased arterial stiffness with significantly higher PWV compared with the normal-BMI group (men: P=0.001; women: P=0.026), which remained after adjustment. In men with low BMI, PWV correlated negatively with BMI before (r - 0.204; P=0.012) and after (r - 0.200; P=0.020) adjustment. Forward stepwise regression analyses indicated a negative association between PWV and BMI in African men. A J-curve was evident suggesting a detrimental effect of low BMI on cardiovascular function in Africans. A low BMI may contribute to the high prevalence of cardiovascular-related morbidity and mortality within a developing country.

Key words: Africans: Cardiovascular function: Low BMI

Low socio-economic status and living in low socio-economic settlements in South Africa are related to non-communicable diseases such as $\text{CVD}^{(1-6)}$. In low socio-economic status communities, a prudent, low-energy, low-fat and micro-nutrient-deficient diet is followed traditionally⁽⁷⁾. The current acculturation process in these settlements is further characterised by detrimental behavioural lifestyle factors such as unhealthy dietary habits, alcohol abuse and smoking, leading to a dramatic increase in $\text{CVD}^{(7-12)}$. This 'new epidemic' of CVD is disproportionally high in poor urban and rural communities⁽⁶⁾.

In the low socio-economic status communities in the North West Province of South Africa, it is striking that African men showed the lowest BMI compared with African women and Caucasian men and women^(13,14). In the Transition and Health during Urbanization of South Africans study, BMI is significantly lower in African men compared with African women (20·8 v. 26·1 kg/m²) as well as the body fat percentage (20·6 v. 47·1%) at all levels of transition^(14,15). In the South African study regarding the influence of Sex, Age and Ethnicity on Insulin sensitivity and Cardiovascular function, African men have also been shown to have a significantly lower mean BMI

than African women as well as Caucasian men and women⁽¹³⁾. In another sub-study of the PURE (Prospective Urban and Rural Epidemiology) study, African men have also been shown to have the lowest BMI values compared with African women⁽⁹⁾.

There has been much emphasis on high BMI as a risk factor for CVD⁽¹⁶⁻²⁰⁾; however, there has been less focus on CVD risk with low BMI⁽²¹⁻²³⁾. A study conducted in Japan has shown that a BMI range of $21-23 \text{ kg/m}^2$ has the lowest morbidity and mortality⁽²⁴⁾. In contradiction, a low BMI has been found to be an independent predictor of cardiovascular events in elderly⁽¹⁷⁾ and in hypertensive patients⁽²⁵⁾, and a J-curve seems evident between BMI and the risk for $CVD^{(17,23,25-27)}$. Low BMI and the association with mortality have often been explained as being due to confounders such as smoking or a pre-existing illness⁽¹⁷⁾. However, studies that controlled for these confounders have still found a J-shaped relationship^(17,22,24,26). The underlying mechanism of this relationship remains unclear. The aim of the present study was, therefore, to investigate the possible associations of low BMI with markers of vascular function in Africans.

Abbreviations: CRP, C-reactive protein; DBP, diastolic blood pressure; GGT, γ -glutamyl transferase; PURE, Prospective Urban and Rural Epidemiology; PWV, pulse wave velocity; SBP, systolic blood pressure.

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Methods

Study design, participants and experimental protocol

The PURE study is a prospective cohort study that tracks changing lifestyles, risk factors and chronic disease using periodic standardised data collection in urban and rural areas of sixteen countries in transition⁽²⁸⁾.

This cross-sectional sub-study is part of the overarching PURE study and was performed in the North West Province of South Africa. The inclusion criteria were eligible residents of the households approached with an apparently low socio-economic status, older than 35 years and with no selfreported chronic diseases or medication. The present study composed of 96% of the participants who were disposed of no formal education or only a basic primary education. The average daily income is less than 3.00 US dollar. As participants were recruited from one of the nine provinces of South Africa and only 21% were employed, the present study may not be representative of the entire black South African population. However, a total of 2010 Africans were recruited from a sample of 6000 randomly selected households in rural and urban setting during the year 2005. All measurements were done in the morning, and subjects were informed about the objectives and procedures of the study before participation. Trained field workers assisted and were available to provide information on participants' language of preference (Setswana-speaking).

The exclusion criteria for this sub-study were participants aged 65 years and older, a history of tuberculosis or HIV infected, an ear temperature higher than 37°C, blood donors and individuals vaccinated in the past 3 months. HIV status was determined with the First Response (PMC Medical) rapid HIV card test using whole blood. If tested positive, the test was repeated with the Pareekshak (Bhat Bio-tech Private Limited) card test, and if positive the participants were referred to their local clinics.

For this sub-study, these subjects were further subdivided into two groups. The optimal BMI for longevity fell between 20·5 and 24·9 kg/m² for men and women⁽²⁹⁾. Therefore, the first group consisted of Africans with a low BMI smaller or equal to 20 kg/m^2 (men *n* 152, women *n* 94) while the second group consisted of Africans with a normal BMI larger than 20 kg/m^2 and smaller or equal to 25 kg/m^2 (men *n* 100, women *n* 150). The remaining participants had BMI larger than 25 kg/m^2 and were only used to illustrate the J-curve effect in overweight and obese subjects compared with normal- and low-BMI subjects.

Ethical considerations

An informed consent form was signed by all the participants before the commencement of measurements. Permission for the execution of the present study was obtained from the provincial Department of Health, the local authorities as well as the tribal Chief from the specific rural area. The study protocol complies with the Declaration of Helsinki as revised in 2008, and was approved by the Ethics Review Board of the North-West University, Potchefstroom, South Africa.

Questionnaires

The participants were interviewed using structured demographic, socio-economic and lifestyle questionnaires developed and standardised for the international PURE study⁽²⁸⁾. Lifestyle data included self-reported current smoking, alcohol consumption as well as medical history.

Anthropometric measurements

Anthropometric measurements were done in duplicate by registered biokineticists and their mean was used. Standardised procedures were used to measure the height (Invicta Stadiometer, IP 1465), weight (Precision Health Scale; A & D Company), and hip and waist circumference of each participant (Holtain unstretchable metal tape) with the guidelines as indicated by Marfell-Jones *et al.*⁽³⁰⁾.

Cardiovascular measurements

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) measurements were obtained with the validated Omron HEM-757 device. Totally, two blood pressure measurements were performed on the right arm (brachial artery), with a 5 min rest period between the two measurements, from which the last value was used while the participants were seated upright and relaxed. The carotid-radial pulse wave velocity (PWV) as a measure of arterial stiffness was determined on the left side of each participant with the Complior SP device (Artech-Medical).

Blood and serum samples

Fasting blood samples were obtained from the antebrachial vein using a sterile winged infusion set and syringes. Serum was prepared according to appropriate methods and stored at -80° C. In the remote areas, serum was stored under dry ice (no longer than 5 d) until it could be transported to the laboratory facility.

Biochemical analyses

Quantitative determinations of total cholesterol, HDL-cholesterol, TAG, γ -glutamyl transferase (GGT) and high-sensitivity C-reactive protein (CRP) were measured utilising the Sequential Multiple Analyzer Computer Konelab20iTM auto-analyzer (Thermo Fisher Scientific Oy).

Data analyses

Data analyses were performed using the Statistica 10 software (StatSoft, Inc.). The population effect size was calculated for PWV as the main outcome measure. The priori analysis calculated that an n value or a population of seventy-eight per group is sufficient to test the hypothesis of the present study.

Non-Gaussian distributions were normalised by logarithmic transformation. *t*-Tests were used to determine significant differences between groups and presented as arithmetic



Fig. 1. Pulse wave velocity (PWV) and diastolic blood pressure (DBP) as a function of BMI, adjusted for age, smoking and consumption of alcohol. Dotted line on the *x*-axis indicates cut-off point for overweight BMI. ----, Men; -----, women.

means with standard deviations or geometric means and 5th–95th percentile intervals. The χ^2 test was used to compare the proportions. One-way ANCOVA was used to determine the differences between BMI groups while adjusting for age, smoking and alcohol consumption, and the differences were presented as mean with 95% CI. The Pearson correlations as well as partial correlations were performed. Partial correlations were adjusted for age, smoking and alcohol consumption or age, smoking, GGT and CRP. PWV was additionally adjusted for mean arterial pressure ((SBP -DBP(0.33 + DBP) and heart rate. Partial correlation analyses were also performed between cardiovascular (SBP, DBP and PWV) and biochemical (GGT and CRP) measures while adjusting for age. Multiple regression analyses using the forward stepwise method were used to determine independent associations between cardiovascular variables and BMI in each sex and BMI group. Significant values were noted as $P \le 0.05$. Fig. 1 is determined by calculating the average value for each BMI value expressed as a whole number.

Results

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Characteristics of the participants

The group was stratified into low- and normal-BMI groups. The age distributions of the groups were similar. As expected, the low-BMI men and women showed lower BMI and waist circumference values (Table 1). Men with low BMI, compared with those with normal BMI, showed significantly higher DBP (P=0.022) and higher PWV (P=0.001). In women, the low-BMI group had a higher PWV compared with the normal-BMI group (P=0.026). Men with low BMI had lower total cholesterol (P=0.036) as well as TAG (P=0.002) and higher CRP (P=0.016) values compared with the normal-BMI group. The low-BMI group smoked more and consumed more alcohol (men 74.3, 70.4% and women 67, 46.8%, respectively).

After adjusting for age, smoking and alcohol consumption and PWV additionally adjusted for mean arterial blood pressure and heart rate, DBP and PWV remained significantly higher in men with low BMI compared with the normal-BMI men (Table 2). Women with low BMI also sustained a significantly higher value for PWV compared with the normal-BMI group. Table 1. Characteristics of study population with low and normal BMI (kg/m^2)

(Arithmetic mean values and standard deviations; geometric mean values and 5th-95th percentiles; number of participants and percentages)

	Low BMI (BMI \leq 20 kg/m ²) (<i>n</i> 152)		Normal BMI (20 $<$ BMI \leq 25 kg/m ²) (<i>n</i> 100)		
Variable	Mean	SD	Mean	SD	Р
Men					
Age (years)	47.9	8.06	49.7	7.3	0.078
BMI (kg/m²)	17.9	1.41	21.8	1.27	<0.001
WC (cm)	69.8	5.55	78·9	4.97	<0.001
Weight (kg)	50.0	5.73	61.4	6.10	<0.001
Cardiovascular variables					
SBP (mmHg)	135.5	19.5	131.7	18.3	0.122
DBP (mmHg)	88.0	13.4	84.2	12.2	0.022
MAP	103.4	17.2	100.9	16.7	0.082
PWV (m/s)	12.6	2.47	11.6	2.00	0.001
HR (bpm)	71.4	18.2	65.8	13.9	0.009
Biochemical variables GGT (units/l)		_		_	0.679
Geometric mean	75	.9	70	70.8	
5th-95th percentile	22.4-	489.8	22.9-	436-8	0.010
CRP (mg/l)		20			0.016
Geometric mean	2.6	59	1.8	14 10 7	
TC (mmol/l)	1 00	-0000 1 / 1	0.29- 5 10	1 26	0.026
	4.02	0.20	1 20	1.06	0.000
Lifestyle factors	0.99	0.30	1.30	1.00	0.002
Smoking					0.011
n	11	3	5	9	0011
%	74	.3	5	9	
Alcohol consumption		0			0.062
n	107 59				
%	70.4 59				
Women					
Age (years)	47.8	7.15	48.9	7.77	0.269
BMI (kg/m ²)	17.7	1.75	22.7	1.37	<0.001
WC (cm)	64.3	4.20	74.3	5.72	<0.001
Weight (kg)	43.5	5.41	56.6	5.72	<0.001
Cardiovascular variables					
SBP (mmHg)	126.8	21.1	127.0	20.8	0.944
DBP (mmHg)	85.9	13.7	85.6	14.4	0.888
MAP	100.0	17.5	97.9	17.2	0.163
PWV (m/s)	11.3	2.43	10.6	2.10	0.026
HR (bpm)	77.6	18.7	75.4	14.8	0.296
Biochemical variables					0.000
	50	~	F 4	~	0.393
Geometric mean	56.2 51.3		·3 467 7		
CPR (mg/l)	10.5-	400.1	17.4-	407.7	0 270
Geometric mean	2.9	21	1.0	5	0.370
5th-95th percentile	0.19_	-48.9	0.25-	-28.6	
	5.10	1.46	5.17	1.36	0.715
	1.17	0.61	1.32	0.77	0.137
Lifestyle factors			. 02		5 107
Smoking					0.028
n	6	3	78		
%	67	·0	52.7		
Alcohol consumption					0.046
n	4	4	5	1	
%	46	.8	34	.0	

WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial blood pressure; PWV, pulse wave velocity; HR, heart rate; GGT, γ-glutamyl transferase; CRP, C-reactive protein; TC, total cholesterol. Table 2. Adjusted variables (ANCOVA) with low and normal BMI (kg/m²)*

(Mean values and 95% confidence intervals)

Variables	L (BMI	ow BMI ≤20 kg/m²)	Normal BMI (20 < BMI \leq 25 kg/m ²) n 100		
		n 152			
	Mean	95 % CI	Mean	95 % CI	Р
Men					
Cardiovascular variables					
SBP (mmHg)	135.7	132.8, 138.5	131.5	128.0, 135.0	0.074
DBP (mmHg)	88.0	86.0, 90.0	84.2	81.8, 86.6	0.019
PWV† (m/s)	12.5	12.1, 12.9	11.7	11.3, 12.2	0.01
Biochemical variables					
CRP (mg/l)	2.74	2.32, 3.26	1.94	1.58, 2.43	0.037
TC (mmol/l)	4.85	4.63, 5.07	5.17	4.89, 5.45	0.08
TAG (mmol/l)	0.99	0.86, 1.11	1.31	1.16, 1.46	0.00
	n 94		n 150		
Women					
Cardiovascular variables					
SBP (mmHg)	126.6	122.5, 130.7	127.5	124.2, 130.8	0.730
DBP (mmHg)	85.5	82.7, 88.3	86.0	83.8, 88.2	0.791
PWV† (m/s)	11.3	10.8, 11.7	10.7	10.3, 11.0	0.046
Biochemical variables					
CRP (mg/l)	2.22	1.82, 2.72	1.96	1.65, 2.31	0.900
TC (mmol/l)	5.12	4.83, 5.41	5.16	4·91, 5·38	0.848
TAG (mmol/l)	1.17	1.03, 1.33	1.32	1.20, 1.43	0.115

SBP, systolic blood pressure; DBP, diastolic blood pressure; PWV, pulse wave velocity; CRP, C-reactive protein; TC, total cholesterol.

* Adjusted for age, smoking and alcohol consumption.

† PWV was additionally adjusted for mean arterial pressure and heart rate.

Single and partial regression analyses

In men with low BMI, PWV correlated negatively with BMI before (r - 0.204; P=0.012) and after (r - 0.200; P=0.020)adjusting for age, smoking, alcohol consumption, mean arterial pressure and heart rate (Table 3). A negative association was also evident in men with normal BMI after adjusting for the above-mentioned covariates (r - 0.228; P=0.041). When alcohol consumption was substituted with GGT and CRP in the adjustment, the negative correlation between PWV and BMI was still evident (r - 0.199; P < 0.001) in the low-BMI men, but disappeared in the normal-BMI men. Correlations for SBP (r 0.14; P=0.037) and DBP (r 0.14; P=0.044) with BMI emerged in the normal-BMI men (data not shown). No correlation was found between the cardiovascular (SBP, DBP and PWV) and biochemical variables (GGT and CRP) for both BMI groups, except for DBP and GGT in the normal-BMI men ($r \ 0.170$; P=0.012). In men with low BMI, GGT also showed a negative correlation with BMI before (r - 0.182; P = 0.031) and after adjustments (r - 0.181;P=0.034) were made.

For women, no correlations were found between PWV and BMI in the low- and normal-BMI groups. In women with low BMI, CRP correlated negatively with BMI before (r - 0.381; P=0.001) and after (r - 0.344; P=0.001) adjusting for age, smoking and alcohol consumption. There were also correlations between blood pressure and GGT (P<0.01) in the low- and normal-BMI groups.

In Fig. 1, the variables PWV and DBP expressed as a function of BMI, and tend to reveal a typical J-curve pattern, particularly in African men.

Linear multiple stepwise regression analyses of African men confirmed the negative association between PWV and BMI (adjusted R^2 0.113, $\beta = -0.246$, 95% CI -0.351, -0.141; $P \le 0.001$) in the low-BMI group and (adjusted R^2 0.106, $\beta = -0.146$, 95% CI -0.279, -0.013; P = 0.034) in the normal-BMI group.

Discussion

The present study showed a higher PWV in the low-BMI group compared with the normal-BMI group in both men and women and an inverse relationship between PWV and BMI in men with low BMI. In women, the inverse association between PWV and BMI was absent in the low-BMI group but a tendency existed in the normal-BMI group. This relationship, particularly in African men, is illustrated by a typical J-curve pattern when PWV and DBP are expressed as a function of BMI. Increased arterial stiffness is reflected by an increase in PWV, and arterial stiffness is an independent predictor of adverse cardiovascular events, including mortality^(31,32).

Opposing studies have criticised that some studies have found an increased risk associated with a low BMI but failed to exclude smokers and people with coexisting illness⁽²⁹⁾. After adjusting for smoking and alcohol consumption and the exclusion criteria of the present study, which included

Low BMI Normal BMI

Table 3. Adjusted regression analyses of low and normal BMI (kg/m²)

as independent variable with cardiovascular and biochemical variables

SBP, systolic blood pressure; DBP, diastolic blood pressure; PWV, pulse wave velocity; GGT, y-glutamyl transferase; CRP, C-reactive protein.

* Partial correlations were adjusted for age, smoking and alcohol consumption.

† PWV was additionally adjusted for mean arterial pressure and heart rate.

participants infected with tuberculosis and HIV, or suffering from other self-reported chronic diseases, the negative association between PWV with low BMI still existed, most prominently in African men. The lipid profile is also favourable in Africans, in general, as well as in the present study population.

In support of this, a significant negative association has also been found between GGT and BMI in African men. Although lifestyle factors alone could not explain the present results, because we did not find a direct link between lifestyle or inflammation and arterial stiffness in men, these detrimental lifestyle factors could have a long-term harmful effect on the cardiovascular system and overall health. In women, a link between GGT and blood pressure existed, but although the level of PWV was higher in the low-BMI group, negative correlations between PWV and BMI were not found. As shown previously, behavioural lifestyle and environmental factors such as unhealthy dietary habits, smoking and alcohol consumption have been associated with hypertension and vascular dysfunction in Africans living in low socio-economic conditions^(3,7,9,11).

This higher level of arterial stiffness was accompanied with increased levels of DBP and CRP in men with low BMI. Increased vascular resistance could at least partly contribute to the increased DBP, while inflammation can be associated with CRP⁽³³⁾. This suggests detrimental changes in vascular and endothelial functions in men with low BMI. Low BMI in African people may be the result of environmental factors, which, in turn, may have had a detrimental effect on vascular function. The increased arterial stiffness in low-BMI group may be due to several changes in the vascular wall occurring simultaneously over a long period, including changes in extracellular matrix and endocrine or paracrine factors^(32,33). The relationship between body weight and mortality supports the hypothesis of a curvilinear relation, in which the CVD risk is increased among low- and high-BMI subjects^(17,22,25,27,29).

In accordance with these findings, it is also evident from the literature that serum GGT has conventionally been used as a marker of alcohol consumption and as a non-specific marker of liver function. Furthermore, it is increasingly regarded as a marker of CVD and the conditions associated with CVD such as oxidative stress, leading to a reduced bioavailability of NO^(7,34-36). Wannamethee *et al.*⁽³⁶⁾ indicated that GGT associates with PWV in a prospective study of 6997 men aged 40-59 years with no history of CVD or diabetes. Whether high alcohol consumption or oxidative stress is responsible for this harmful effects in African men remains uncertain; however, both could have an added negative influence on vascular stiffness and vascular damage contributing to CVD^(36,37). These associations suggest that PWV (arterial stiffness), DBP (pre-hypertension) and GGT (oxidative stress) in African men and in a lesser extent in African women play a possible role in predicting impeded cardiovascular function with low BMI, supporting the J-curve theory.

The present study must be further interpreted within the context of its limitations. In the present study, causality could not be inferred. There is a need to compare data obtained from Africans with data from Caucasians. This was a cross-sectional study and because of the focus of the PURE study, participants were selected from specific rural and urban environments from the North West Province of South Africa only, and the present results may not necessarily be representative of the general South African population. We could also not exclude selection biases in this low socioeconomic environment. Contextual variables of sociological interest were not measured. Furthermore, there may be measurement errors, even though all variables were obtained under controlled conditions. For the present study the carotidradialis PWV was measured instead of the carotid-femoralis PWV, the gold standard for measurements of stiffness. Finally, although the present results were consistent after multiple adjustments, we cannot exclude residual confounding.

In conclusion, a detrimental effect of low BMI is evident on cardiovascular function in Africans even after excluding participants with known chronic disease and adjusted for age,

	$(BMI \le 2)$	20 kg/m²)	$(20 < BMI \le 25 \text{ kg/m}^2)$			
Dopondopt	<i>n</i> 1	152	<i>n</i> 100			
variables	Single	Partial	Single	Partial		
Men						
SBP (mmHg)						
r	0.141	0.156	0.061	0.030		
Р	0.083	0.069	0.548	0.777		
DBP (mmHg)						
r	-0.029	- 0.025	0.047	0.048		
Р	0.723	0.767	0.645	0.655		
PWV† (m/s)						
r	-0.204	-0.200	-0.172	-0.228		
P	0.012	0.020	0.093	0.041		
GGT (units/l)						
r	-0.182	-0.181	-0.0123	-0.124		
P	0.031	0.034	0.236	0.244		
CRP (mg/l)						
r	-0.024	-0.021	0.100	0.109		
P	0.778	0.812	0.339	0.304		
	п	94	n 150			
	Single	Partial	Single	Partial		
Women						
SBP (mmHg)	0.001	0.170	0.040	0.054		
r	0.091	0.179	0.046	0.054		
	0.381	0.098	0.575	0.527		
	0.042	0 112	0.001	0.017		
P	0.684	0.302	0.001	0.8/1		
PW/V + (m/c)	0.004	0.302	0.991	0.041		
r vv v j (11/3)	-0.035	-0.042	_0.157	-0.153		
P	0.743	0.708	0.065	0.133		
, GGT (units/l)	0-7-10	0.700	0.000	0.019		
r	-0.187	-0.172	0.008	0.045		
, P	0.077	0.112	0.929	0.601		
, CBP (ma/l)	0.011	0112	0.020	0.001		
r	- 0.381	-0.344	0.055	0.053		
, P	0.001	0.001	0.515	0.533		

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smoking and alcohol consumption. When BMI decreases from the optimum value to lower values, a J-curve is evident⁽²³⁾. PWV, DBP and GGT increased significantly in African men with low BMI, whereas the key J-curve was indicated for the PWV, thus supporting the theory that stiffening of the arteries is evident in Africans with a low BMI. Low BMI may contribute to the high prevalence of CVD mortality within low-income countries such as South Africa and therefore increased the risk for CVD.

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