Cardiovascular Topics

Arterial stiffness assessment in obese black South African patients

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Abstract

Introduction: Increased arterial stiffness is a determinant of cardiovascular mortality and an independent marker of cardiovascular disease. The objective of this study was to asses arterial elasticity by determination of pulse-wave velocity (PWV) and augmentation index (Aix) in obese black patients.

Methods: PWV and Aix were assessed non-invasively using the AtCor SphygmoCor® system (AtCor Medical, Inc, Sydney, Australia). The study participants were divided into four groups; healthy volunteers (HV) (n = 29), patients with concomitant diseases but normal body mass index (Nd) (n = 23), obese patients without concomitant diseases (OB) (n = 29) and obese patients with concomitant diseases (OBd) (n = 29).

Results: The difference in the mean levels of PWV was statistically significant in the obese group with and without concomitant disease. The PWV in the OB group (7.9 ± 2.9 m/s) and in the OBd group (9.2 ± 4.4 m/s) was, respectively, 19.7 and 33.3% higher than in the HV group (6.6 ± 2.1 m/s). PWV was directly correlated with age, glycated haemoglobin level, aortic systolic blood pressure and heart rate. The risk of cardiovascular diseases in the obese patient without additional diseases was increased by 50.7%. The presence of concomitant diseases (type 2 diabetes mellitus and hypertension) in addition to obesity increased arterial stiffness by a further 11.4% and therefore also increased the risk of cardiovascular diseases by a further 35.1%. Aix was increased in the OBd and Nd groups by 8.2 and 16.5%, respectively, however the increase was not statistically significant. Aix was directly correlated with age, heart rate and aortic systolic blood pressure.

Conclusion: The obese black patients had a higher PWV, indicating increase in arterial stiffness and therefore a higher risk for cardiovascular disease. In addition, aging, increased blood pressure and type 2 diabetes mellitus contributed further to arterial stiffening in these obese patients.

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Arterial stiffening is the ongoing loss and fragmentation of elastin, and an accumulation of stiffer collagen fibres in the arterial wall.[1] Arterial stiffness increases with aging and concomitant diseases such as diabetes mellitus, atherosclerosis, hypertension, chronic kidney disease and stroke.[2,3]

Obesity is linked with a high risk of cardiovascular disease (CVD), particularly when body fat is distributed within the abdominal region. When compared with non-obese subjects, obese subjects have increased arterial stiffness.[4,5]

Pulse-wave velocity (PWV) and augmentation index (Aix) are gold-standard, non-invasive markers of arterial elasticity and predictors of cardiovascular morbidity and mortality.[6] PWV is a direct measure of large-artery stiffness. Aix is a surrogate measure of arterial rigidity that could be influenced by the left ventricular ejection fraction and peripheral haemodynamics, as well as the properties of the large arteries.[7]

PWV values are calculated from the time interval between the estimated forward and reflected waves and are comparable with invasive measurements. Aix values are calculated as the ratio of the augmentation pressure to the pulse pressure.[8] A slow PWV indicates good elasticity and a fast PWV, poor elasticity.[9] A 1-m/s increase in aortic PWV has been shown to equate to 39% increase in risk of cardiovascular events.[10] PWV is an independent predictor of stroke and coronary heart disease in healthy subjects.[11] Aix, a measure of pulse-wave reflection, is a more direct measure of arterial stiffness. It calculates how much of the central pulse pressure is accounted for by the reflected pulse wave.[12]

Elevated PWV and Aix are associated with poor cardiovascular health.[13] Increased PWV and Aix indicate damage to the elastic tissue of the arteries.[14] Various studies have reported the effects of obesity on arterial elasticity in different ethnic groups.[15,16]

The aim of this study was to assess arterial stiffness in obese black South African patients. The objectives of the study were to compare the difference in arterial stiffness and to evaluate the effect of hypertension and diabetes on arterial stiffness in obese and non-obese patients using PWV and Aix analysis. This study is the first to assess the effects of obesity on arterial stiffness in obese black South African patients.

Methods

The study was approved by the Sefako Makgatho University Research and Ethics Committee (SMUREC/M/112/2016:PG). Informed consent was obtained from the participant before entering the study. Full explanation of the procedure was given with the possibility of withdrawal at any time. The study was conducted in accordance with the principles detailed by the Declaration of Helsinki.

A comparative study model was used and 110 participants were recruited from the Sefako Makgatho Health Sciences University community. Body mass index (BMI) groups were categorised according to the World Health Organisation's nutrition/BMI guidelines and defined as a person's weight in kilograms divided by the square of the person's height in metres. Below 18.5 kg/m^2 was defined as underweight, 18.5–24.9 kg/m^2 as normal, 25.0–29.9 kg/m^2 as pre-obesity, 30.0–39.9 kg/m^2 as obese and above 40 kg/m^2 as severe obesity.

The study participants were divided into four groups; healthy volunteers (HV) (n = 29), patients with concomitant disease (type 2 diabetes mellitus and hypertension) but normal BMI (Nd) (n = 23), obese patients without concomitant disease (OB) (n = 29), and obese patients with concomitant disease (OBd) (n = 29).

The eligibility criteria for healthy volunteers were male or female, aged 18–70 years with no abnormalities in the physical examination and no chronic or acute diseases (not on any chronic medication). The eligibility criteria for the study patients were male or female, aged 18–70 years, with type 2 diabetes and with or without hypertension, with a BMI ≤ 25 kg/m^2 and on metformin as monotherapy or metformin plus sulfonylurea as a dual combination therapy plus hypertensive therapy (enalapril 10 mg and/or hydrochlorothiazide 12.5 mg) if needed. The obese patients were not on any medications used to treat hyperlipidaemia. No additional medication (and no withholding of medication) was given to the patients with diabetes or other concomitant diseases.

The exclusion criteria were patients with type 1 diabetes mellitus, a history of ketoacidosis, current treatment with all types of insulin, patients acutely ill or unstable, and patients with poorly controlled concomitant chronic diseases, such as systolic blood pressure (SBP) ≥ 160 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg.

Sample size calculations were based on estimation of the difference in PWV between any two groups. With a sample size of 26 per group, a two-sided t-test at the 5% level would have 80% power to detect a difference of 2 m/s (7–9) in PWV between any two groups, assuming a common standard deviation of 2.5 m/s. Sample size calculation was done on Query Advanced (Statistical Solution Ltd, Cortc, Ireland), version 8.1.1.0.

Questionnaires were completed, and vital signs, BMI and fasting glucose levels were measured. After overnight fasting, venous blood was collected via vacupunture and determination of glycated haemoglobin (HbA_{1c}) levels and lipid profiles was done by the National Health Laboratory Services, which is a South African National Accreditation System (SANAS) accredited laboratory. The National Health Laboratories Services handbook on standard operating procedures, version 1, active from 6 March 2015, and document number GPQ0064, was used as a guideline to ensure correct and consistent sample collection and handling. Other variables such as smoking and alcohol consumption were recorded.

Validity was maintained by strict adherence to the inclusion and exclusion criteria. The AtCor SphygmoCor®, used for measuring PWV and Aix, was operated by a trained, dedicated user. All of the apparatus used in the laboratory investigations were acquired from reputable suppliers and the procedures were conducted according to the manufacturer's protocol.

PWV and Aix were assessed non-invasively using the AtCor SphygmoCor® system (AtCor Medical, Inc, Sydney, Australia). Electrocardiogram-gated carotid and femoral waveforms were recorded using applanation tonometry. Carotid–femoral path length was measured as the difference between the surface distance joining (1) the suprasternal notch, the umbilicus and the femoral pulse, and (2) the suprasternal notch and the carotid pulse. The carotid–femoral transit time was estimated in eight to 10 sequential femoral and carotid wave forms as the average time difference between the onset of the femoral and carotid waveforms. PWV was calculated as the carotid–femoral path length divided by the carotid–femoral transit time as expressed in metres per second.[9]

Aix was measured by pulse-wave analysis (PWA). Radial artery waves were recorded non-invasively by applanation tonometry. Twenty waves were captured and PWA was used to derive a central aortic pulse wave and haemodynamic measures by a generalised validated mathematical transfer function. Aix measurements were standardised to a pulse rate of 75 beats per min and expressed as a percentage (%).[12] Assessment of arterial elasticity by determination of PWV and Aix was done in the obese black patients.

Statistical analysis

All statistical analyses were done on SAS (SAS Institute Inc, Carey, NC, USA). Continuous variables are summarised as mean values and standard deviations. Mean values of the demographic variables were compared between the four test groups by analysis of variance (ANOVA) followed by pairwise t-test comparison. Median values for both PWV and Aix were calculated. Linear regression analysis was performed with PWV and Aix @75 as outcomes (dependent) variables and the demographic variables as predictors (independent) variables.

Results

Of the 110 study participants, 29 were healthy volunteers aged 37.2 ± 10 years, 23 patients were non-obese with concomitant disease (type 2 diabetes mellitus and hypertension), aged 58.8 ± 8.4 years, 29 patients were obese without concomitant disease, aged 44.2 ± 14.6 years, and 29 patients were obese with concomitant disease, aged 53.1 ± 9 years.

The clinical and haemodynamic characteristics of the study participants are shown in Table 1. The average BMI was 24.82 ± 1.9 kg/m^2 for the HV group, 24.7 ± 2.4 kg/m^2 for the Nd group, 35.4 ± 4.2 kg/m^2 for the OB group and 35.4 ± 4.9 kg/m^2 for the OBd group. All the participants in the OBd and Nd groups additionally had type 2 diabetes mellitus, and 65.2% of the Nd group and 75.9% of OBd group had concomitant hypertension (Table 1).

The mean PWV levels were statistically significantly different in the obese group with and without concomitant disease. The PWV in the OB group (7.9 ± 2.9 m/s) and in the OBd group (9.2

Table 1. Characteristic of the study participants (n = 110)

Variables	*HV* (n = 29)	*Nd* (n = 23)	*OB* (n = 29)	*OBd* (n = 29)
Age, years	37.21 ± 10.19	58.79 ± 8.43*	44.17 ± 14.63*	53.14 ± 9.99*#
BMI, kg/m²	24.8 ± 1.9	24.7 ± 2.35	35.41 ± 4.20*	35.41 ± 4.87*
Diabetes mellitus, %	–	100	–	100
Current smoking, %	10.3	8.7	10.3	13.8
Hypertension, %	–	65.2	–	75.9
Heart rate, bpm	68.62 ± 9.66	70.48 ± 14.16	68.86 ± 12.13	73.52 ± 10.63
Aortic PP, mmHg	32.93 ± 9.33	46.17 ± 18.81*	41.24 ± 16.58	45.62 ± 20.46*
Radial PP, mmHg	41.241 ± 10.63	60.04 ± 18.50*	50.59 ± 15.11*	56.89 ± 21.23*
MAP, mmHg	90.79 ± 11.30	101.13 ± 13.63*	96.89 ± 9.7*	104.83 ± 11.73*#
Aortic SBP, mmHg	107.45 ± 16.05	129.00 ± 19.06*	118.28 ± 14.25	128.17 ± 21.28*#
Aortic DBP, mmHg	76.48 ± 8.6	80.913 ± 10.32*	79.62 ± 6.68*	84.62 ± 9.52*
Radial SBP, mmHg	117.28 ± 17.74	138.87 ± 19.15*	127.52 ± 14.51*	138.66 ± 22.84*#
Radial DBP, mmHg	72.69 ± 10.59	79.35 ± 10.52*	78.41 ± 6.29*	83.28 ± 9.28*#
HbA_{1c}	5.06 ± 0.32	8.78 ± 2.12*	5.93 ± 1.45	11.25 ± 8.68*#
TC	4.61 ± 1.35	5.00 ± 1.28	4.94 ± 1.06	4.56 ± 1.11
LDL-C	3.07 ± 1.41	3.20 ± 1.20	3.14 ± 0.95	2.82 ± 0.86
HDL-C	1.26 ± 0.25	1.28 ± 0.33	1.15 ± 0.18	1.24 ± 0.37
TG	1.07 ± 0.56	1.23 ± 0.64	1.50 ± 1.27	1.81 ± 1.37*
Aix, %	24.241 ± 15.14	28.26 ± 10.26	23.48 ± 10.90	26.24 ± 8.52
PWV, m/s	6.59 ± 2.18	7.87 ± 3.61	7.93 ± 2.94	8.80 ± 3.30*

BMI, body max index; PP, pulse pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; HbA_{1c}, glycated haemoglobin; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol; TG, triglycerides; Aix, augmentation index; PWV, pulse-wave velocity; HV, healthy volunteers; Nd, non-obese with concomitant disease; OB, obese without concomitant disease; OBd, obese with concomitant disease.
*p < 0.05 HV compared with Nd, OB and OBd, #p < 0.05 OB compared with OBd.

± 4.4 m/s) were, respectively, 19.7 and 33.3% higher (p < 0.05) than in the HV group (6.6 ± 2.1 m/s). The risk of CVD in the obese patient without additional disease was 50.7% higher. The presence of concomitant disease (type 2 diabetes mellitus and hypertension) in addition to obesity increased arterial stiffness further by 11.4% and therefore further increased the risk of CVD by 35.1%.

Aix was higher in the OBd and Nd groups by 8.2 and 16.5%, respectively, however the increase was not statistically significant. Aix was directly correlated with age, heart rate and aortic SBP. Interestingly, Aix did not differ significantly in the OB group when compared to the HV group (Table 1).

The results of this study indicated that PWV and Aix increased with increasing age. The values for PWV and Aix for the four groups by age are shown in Figs 1 and 2.

To identify the variables that were independently correlated with PWV and Aix, a multivariable linear regression analysis including all studied participants (n = 110) was performed (Table 2). PWV was directly correlated with age, aortic SBP, HbA_{1c} level and heart rate. Aix was directly correlated with age, aortic SBP and heart rate, and inversely correlated with radial SBP and radial DBP (Table 2).

The results of this study indicate that age and the presence of concomitant disease was associated with significant differences between PWV and Aix. Interestingly, obese patients without concomitant disease did not show a significant increase in PWV or Aix.

Discussion

Obesity is a recognised independent predictor of CVD and/or mortality.[17,18] Body fat distribution may have an effect on arterial compliance, and increased peripheral artery stiffness is associated with larger abdominal body fat mass.[19] Lentferink *et al.* links obesity with higher arterial pressure and suggests that this might be as a result of an increased preload and afterload due to increased metabolic demand.[20] The authors also suggest that in obese populations it can be anticipated that PWV will be higher if the arterial pressure surpasses the physiological adaptations.[20]

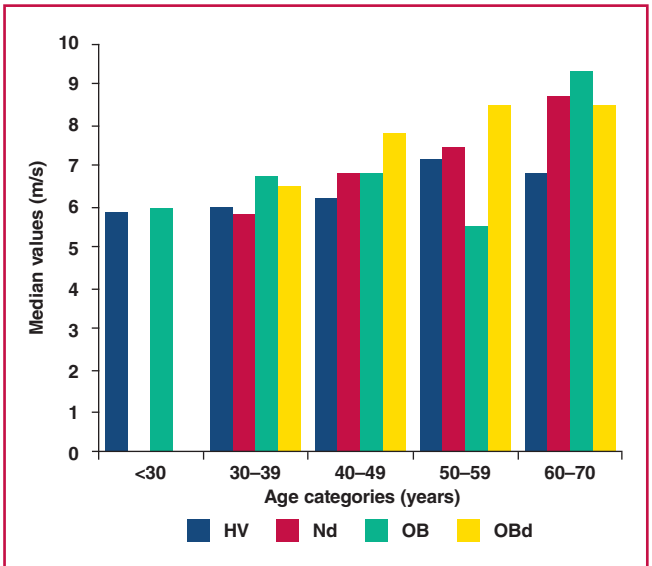

Fig. 1. PWV values for the study participants according to age categories and study groups.

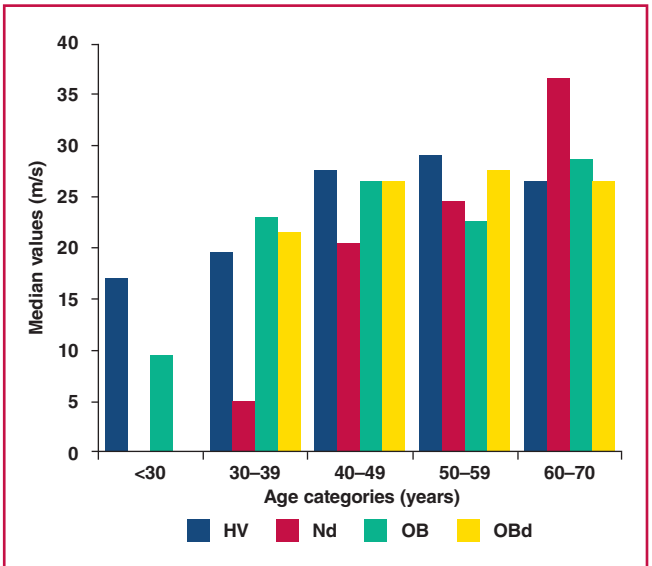

Fig. 2. Aix values for the study participants according to age categories and study groups.

Table 2. Multivariable linear regression analysis for PWV and Aix in the study participants (n = 110)

Variables	*Aix (± SE)*	p-*value*	*PWV (± SE)*	p-*value*
Age	0.156 ± 0.07	0.04*	0.046 ± 0.021	0.031*
Aortic PP	0.11 ± 0.132	0.402	–0.073 ± 0.044	0.101
Radial PP	–0.276 ± 0.161	0.089	0.079 ± 0.534	0.15
MAP	–0.041 ± 0.170	0.081	–0.067 ± 0.56	0.234
Heart rate	0.398 ± 0.081	< 0.0001*	0.060 ± 0.027	0.03*
Aortic SBP	1.595 ± 0.022	< 0.0001*	0.228 ± 0.073	0.003*
Aortic DBP	0.920 ± 0.599	0.135	–0.174 ± 0.197	0.383
Radial SBP	–1.134 ± 0.214	< 0.0001*	–0.097 ± 0.07	0.017
Radial DBP	–1.449 ± 0.524	0.009*	–0,165 ± 0.178	0.357
BMI	–0.045 ± 0.124	0.714	0.07 ± 0.041	0.079
HbA_{1c}	–0.013 ± 0.172	0.940	0.192 ± 0.056	0.0009*
TC	–1.929 ± 1.67	0.251	0.544 ± 0.554	0.329
LDL-C	2.34 ± 1.73	0.183	–0.201 ± 0.577	0.728
TG	–1.51 ± 0.827	0.191	–0.124 ± 0.284	0.664
HDL-C	6.92 ± 3.226	0.054	–0.706 ± 1.07	0.512

MAP, mean arterial pressure; PP, pulse pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body max index; HbA_{1c}, glycated haemoglobin; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; SE, standard error; Aix, augmentation index; PWV, pulse-wave velocity. *$p < 0.05$.

The results of this study indicated that arterial stiffness was increased in these obese patients, however concomitant disease such as hypertension and type 2 diabetes played a major role in arterial stiffness, increasing PWV by 19.7% in the obese patients and by 11.4% in non-obese patients (Table 1).

A 1-m/s increase in aortic PWV has been shown to equate to a 39% increase in risk of cardiovascular events.[9,10] In this study, the risk of CVD in the obese patient without additional disease was increased by 50.7%, and in obese patients with additional diseases, the risk increased by a further 35.1%.

The results of this study show that PWV was directly correlated with HbA_{1c} levels and this is similar to that found by Elias *et al*., where type 2 diabetes mellitus status was linked with a significantly higher PWV.[21] Studies have shown increased stiffening of arteries in diabetes, and this suggests that it might be due to endothelial dysfunction, low-grade inflammation and oxidative stress, as well as the formation of advanced glycation end-products in the vessel wall, causing cross-linking of collagen molecules and loss of elasticity.[22]

Continuous increases in blood pressure also stimulate matrix synthesis, causing subsequent elevation in vascular thickness and structural stiffening.[23] In addition, chronic hyperglycaemia and hyperinsulinaemia elevate the local activity of the renin–angiotensin–aldosterone system and the expression of angiotensin type I receptors in the vascular tissue, resulting in the development of wall hypertrophy and fibrosis.[24]

A study by Osuch *et al*. showed that there was an improvement in arterial elasticity in black patients on angiotensin converting enzyme inhibitors (perindopril 4 mg).[9] It would be warranted to investigate further the influence of angiotensin converting enzyme inhibitors on arterial elasticity in obese populations.

According to previous studies, Aix can be influenced by an individual's age, gender and heart rate.[21] Our study showed that in obese black participants, Aix was significantly correlated with age, aortic SBP, and radial SBP and DBP, indicating that age and increased BP might lead to an increase in arterial stiffness (Table 2). Increased BP upsurges afterload and the oxygen demand of the myocardium and contributes to left ventricular hypertrophy. This leads to increased arterial stiffness, leading to an imbalance between myocardial oxygen demand and supply.[2]

A study by Mittchell *et al*. showed that a healthy individual with no evidence of CVD and low burden of risk factors had age-related increased aortic stiffness.[25] Boutouyrie and Vermeersch showed that the enhanced influence of ageing with high BP was gradual, the increase in PWV with BP was more prominent as the subjects got older and that the correlation between PWV and age was highly significant.[26] This might be due to the remodelling of the middle tunica, comprising the fragmentation of elastin and its replacement with collagen fibres and calcium deposition, resulting in loss of elasticity and decreased arterial compliance.[25,26]

The results of this study concur with a number of studies where arterial stiffness increased with increasing age.[2,22] The results showed that age was directly correlated with PWV and Aix (Table 2) and that PWV and Aix increased with increasing age (Table 2, Figs 1 and 2).

There were limitations to this study. Due to the small sample size, a separate analysis regarding the effect of different antihypertensive and antidiabetic medication on arterial stiffness could not be investigated. The small sample size impacted negatively on the power of the test and therefore it is proposed that the research should be repeated with a larger sample. Anthropometric measurements such as body circumference and waist-to-hip ratio were not done.

Conclusion

Obese black patients had higher PWV, indicating stiffer arteries and therefore higher risk for CVD. The risk of CVD in the obese patient without additional diseases was increased by 50.7%. Furthermore, aging, increased BP, type 2 diabetes mellitus and increased cholesterol level contributed further to arterial stiffening in these obese patients. The presence of concomitant diseases (diabetes and hypertension) increased arterial stiffness by 11.4% and therefore further increased the risk of CVD by 35.1%.

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