Examining waist and neck circumferences as screening tools for metabolic syndrome in a sub-Saharan Caucasian cohort at three year follow-up: the SABPA prospective cohort

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Keywords: metabolic syndrome, anthropometric, waist circumference, neck circumference, sub-Saharan Caucasian

Abstract

Objectives: Waist circumference (WC) cut-off points specific to sub-Saharan Caucasians do not exist with which to identify metabolic syndrome. Neck circumference (NC), as an additional measure, was previously found to be a worthy identifier of metabolic syndrome. Therefore, the aim was to determine NC and WC cut-off points specific to our Caucasian cohort, to confirm baseline cut-off points and to determine whether or not WC cut-off points specific to this cohort differed from the Joint Interim Statement (JIS) WC guidelines.

Design, subjects and setting: A target population study, nested in a prospective cohort, was assessed and included 90 and 96 Caucasian men and women aged 24-65 years from the Dr Kenneth Kaunda Municipality District, North West province.

Outcomes measures: Anthropometric and fasting biological markers for metabolic syndrome, e.g. systolic and diastolic blood pressure, glucose, triglycerides and high-density lipoprotein, were obtained.

Results: Cut-off points were determined with the use of a receiver operating characteristic. With the use of cohort-specific WC cut-offs, metabolic syndrome prevalence did not change. WC cut-off points were 96 cm for men and 88 cm for women. NC cut-off points were 42 cm and 35 cm, for men and women, respectively.

Conclusion: WC cut-off points specific to these Caucasians differed to those from the JIS guidelines, but corresponded with the baseline findings of the prospective cohort. From a clinical perspective, we cautiously suggest the application of NC, rather than WC, as an anthropometric measure of metabolic syndrome in women as it was a stronger predictor of metabolic syndrome and is not influenced by menopausal status *per se*.

Introduction

The Joint Interim Statement (JIS) classification of metabolic syndrome is the most recent definition thereof, but nevertheless requires further refinement in terms of defining waist circumference (WC) measurement in this regard for sub-Saharan Africans.[1] Various studies have been conducted to define WC in sub-Saharan black Africans as a marker of metabolic syndrome.[2-5] However, limited studies define WC in Caucasians from sub-Saharan Africa as an identifier of metabolic syndrome. The Europid WC cut-off points, of 94 cm for men and 80 cm for women, are the only WC measurements that are applicable to sub-Saharan Caucasians, as stated within the JIS and by the International Diabetes Federation.[1,6] According to the JIS, ethnic-specific WC cut-off points need to be developed. Therefore, it is necessary to determine whether or not the suggested European WC cut-off points are applicable to sub-Saharan Caucasians.

With regard to two populations with a similar genetic background, but residing in different areas, findings revealed that environmental factors may have affected anthropometry.[7] Seidell et al[8] added that it is pertinent to develop different WC cut-off points for persons of specific descent and persons of the same descent living in other countries. Therefore, the use of European cut-off points for Caucasians from Africa may not be appropriate in determining metabolic syndrome prevalence, and to our knowledge, only one other study has investigated the WC cut-off point for sub-Saharan Caucasians (WC cut-off points of 97 cm for men and 84 cm for women).[4]

In order to further enrich the use of anthropometry as a screening tool for metabolic syndrome, neck cir-

cumference (NC) cut-off points were also determined. The literature has revealed that NC can be an identifying measure of health risk,[9-10] and that it is a worthy identifier of the presence of metabolic syndrome in sub-Saharan Caucasians.[11]

Findings from the prospective phase of the present Sympathetic Activity and Ambulatory Blood Pressure Study in Africans (SABPA) study suggest that WC cut-off points should be further investigated in sub-Saharan Caucasians, and not just in Africans, as various studies have already investigated the latter.[2-5] WC cut-off points from the current substudy suggest that the European reference values in metabolic syndrome might not be applicable to this specific Caucasian cohort; especially to the women. However, even with substitution of the WC defined by the JIS with the new cohort-specific WC for metabolic syndrome, the prevalence of metabolic syndrome remained similar.

To our knowledge, WC and NC cut-off points specific to metabolic syndrome for sub-Saharan Caucasians have only been investigated by the SABPA cohort.[4-11] Now, at three-year follow-up, it is necessary to confirm these cut-off points and to determine whether or not the cohort-specific anthropometric cut-off points differ from the European reference values (JIS), and hereby address the void in the literature regarding sub-Saharan Caucasians.

Method

Participants

As this was a three-year follow-up, only participants from Phase I (2009) were included, which accounted for a successful follow-up rate of 89%. Exclusion criteria included pregnancy, lactation, a tympanum temperature > 37.5°C, and the use of alpha and beta blockers and psychotropic substance abuse. Blood donors and persons vaccinated in the three months prior to participation were also excluded. The 2012 eligible participants (n = 186) were Caucasian teachers aged 24-65 years, and comprised 90 men and 96 women working in the Dr Kenneth Kaunda District Municipality in North West province, and thus was homogenous with regard to socio-economic class. Participants were fully informed of the procedure, and signed an informed consent form. The study conformed to the ethical principles for medical research involving human subjects of the World Medical Association Declaration of Helsinki (revised 2008) and was approved by the Ethics Review Board of North-West University, Potchefstroom Campus (NWU-00036-07S6).

Procedure

Clinical assessments were performed from late summer until late autumn in 2012 over a two-day period for each participant, as described eslewhere.[12] At 15h00 each day of the working week, four participants were received at North-West University and stayed overnight at the Lipid Clinic and Metabolic Unit research facility on campus. They were introduced to the experimental set-up in order to lessen anticipation stress. Participants received standardised meals for the duration of data collection and were encouraged to go to bed at 22h00, after which they had to fast until the clinical measures were completed the next morning. Measurements commenced the next morning at 07h00, starting with the anthropometric measurements, which were followed by blood pressure and blood sampling. Lastly, in order to assess physical activity, participants were fitted with an Actiheart® Physical Activity Monitor (CamNtech, Cambridge, UK), to be worn over a seven-day period. The epoch was set at 60-second intervals.

Anthropometric measurements

A level 2-accredited anthropometrist recorded the measures in triplicate. Maximum height was measured with a stadiometer to the nearest 0.1 cm, and weight was measured with weight evenly distributed on a Krups® scale to the nearest 0.1 kg. Height and weight was used to calculate body mass index (BMI) (kg/m^2).

Circumferences were taken with a non-extensible and flexible anthropometric tape, using standardised procedures. WC was taken at the midpoint between the lower costal rib and the iliac crest, perpendicular to the long axis of the trunk, and not at the narrowest point, for standardisation purposes. The NC was taken superior to the thyroid cartilage, perpendicular to the long axis of the neck.[13] Inter- and intraobserver variability was less than 10%.

Clinical measurements

Participants were in a semi-recumbent position for 20-30 minutes prior to the blood pressure measurements being taken with a calibrated sphygmomanometer using the Riva-Rocci-Korotkoff method on the non-dominant arm[14] by applying a suitable cuff. Two duplicate measures were taken, with a 3- to 5-minute resting period between each; the second of which was used for statistical analyses.

A registered nurse obtained fasting resting blood samples with a winged infusion set from the brachial vein branches of the dominant arm. Sodium fluoride glucose and serum samples for metabolic syndrome markers were handled according to standardised procedures and stored at -80°C. Analysis was performed using the Konelab™ 20i Sequential Multiple Analyzer Computer (ThermoScientific, Vantaa, Finland) and the timed, end-point method (UniCel® DxC 800, Beckman and Coulter, Germany) at independent accredited laboratories.

Metabolic syndrome classifications

Metabolic syndrome is defined as the presence of three or more of the following risk factors:

- Triglycerides ≥ 1.7 mmol/l.
- High-density lipoprotein (HDL) of 1 mmol/l for men and < 1.3 mmol/l for women.
- Glucose ≥ 5.6 mmol/l.
- Systolic blood pressure ≥ 130 mmHg and/or diastolic blood pressure ≥ 85 mmHg.
- WC for men ≥ 94 cm and for women ≥ 80 cm.[1]

Since WC is the variable for which cut-off points are developed, it therefore cannot be included in this model. Therefore, WC was excluded as a metabolic syndrome component to predict the presence of any two or more of the metabolic syndrome components. The use of two or more components other than WC has been successfully demonstrated in other South African studies.[2-3] In our study, after specific cut-off points were developed, those contained in the JIS definition were substituted with the new cohort-specific cut-off points to determine the prevalence of metabolic syndrome.

Statistical analysis

Data were analysed with SPSS® version 21 for Windows®. Initially, gender-specific descriptive statistics mean, standard deviation and proportions were determined. Thereafter, nonparametric receiver operating characteristic (ROC) curves, together with the area under the curve (AUC) were computed and the optimal cut-off points obtained from the Youden index (J) maximum (sensitivity + specificity - 1). ROC statistics were computed using continuous WC values and categorical values for metabolic syndrome (any two or more factors other than WC) in order to determine the optimal WC cut-off points. ROC statistics were also used to determine NC (continuous values) cut-off points for metabolic syndrome (categorical values). The AUC had to be more than 0.5 and closer to 1, indicating accuracy and not random chance. Adjusting for covariates was not possible during computation of the ROC statistical analysis. The ROC-derived WC cut-off points were then used instead of those contained in the JIS criteria in order to determine the prevalence of metabolic

syndrome (any three or more components). Lastly, in order to determine which metabolic syndrome risk factors contributed the most to metabolic syndrome prevalence, AUC values were determined for each of the metabolic syndrome components (continuous values) using ROC statistics with metabolic syndrome as a categorical value.

Results

According to the JIS criteria, the metabolic syndrome profile of these Caucasian men was vulnerable regarding their HDL, diastolic blood pressure and WC values (Table I). In comparison, as a group, the woman had fewer risk factors for metabolic syndrome, and their low HDL and high WC values indicated metabolic syndrome risk. Although the WC for both the men and women was above the JIS threshold, these WC values might not be applicable to our specific cohort. Therefore, ROC statistics were computed in order to determine the WC cut-off points specific to this Caucasian cohort. The ROC developed WC cut-off points (Figure 1) for men and women, which were 96 cm [AUC 0.63, 95% confidence interval (CI): 0.52-0.75] and 88 cm (AUC 0.61, 95% CI: 0.47-0.76), respectively, while the suggested JIS cut-off points were set at 94 cm for men and 80 cm for women.

Table I: The descriptive statistics of the Caucasian men and women[1]

Descriptive characteristics	Men (n = 90)	Women (n = 96)
Age (years)	49.24 ± 10.19	49.90 ± 9.62
Oestradiol levels (pg/ml)	14.32 ± 9.53	74.32 ± 70.04
Body mass index (kg/m2)	30.24 ± 5.14	27.41 ± 6.85
Physical activity (Kcal/hour)	1 660.04 ± 1 577.93	1 099.45 ± 615.53
Gamma-glutamyl transferase (U/l)	35.66 ± 39.77	19.01 ± 23.73
Self-reported smokers (n) (%)	14 (15.6)	9 (9.4%)
Neck circumference (cm)	42.70 ± 3.23	34.44 ± 2.95
Metabolic syndrome components		
Glucose (mmol/l)	4.69 ± 1.28	4.19 ± 1.17
High-density lipoprotein (mmol/l)	0.85 ± 0.23	1.26 ± 0.37
Triglycerides (mmol/l)	1.42 ± 1.11	0.96 ± 0.55
SBP (mmHg)	128.47 ± 13.25	118.93 ± 11.40
DBP (mmHg)	87.69 ± 9.46	79.10 ± 8.02
Waist circumference (cm)	106.12 ± 106.12	87.03 ± 14.37
Increased blood pressure (either SBP ≥ 130 mmHg and/or DBP ≥ 85 mmHg)*	56 (62.2%)	30 (31.3%)
Medication use		
Diabetic (clinically diagnosed), n (%)	7 (7.8)	3 (3.1)
Hypertension (clinically diagnosed), n (%)	22 (24.44)	15 (15.62)
Statins, n (%)	20 (22.22)	13 (13.54)
Hormone replacement therapy, n (%)	0 (0)	28 (29.17)

DBP: diastolic blood pressure, SBP: systolic blood pressure
Data indicated as mean ± standard deviation
*: According to the Joint Interim Statement
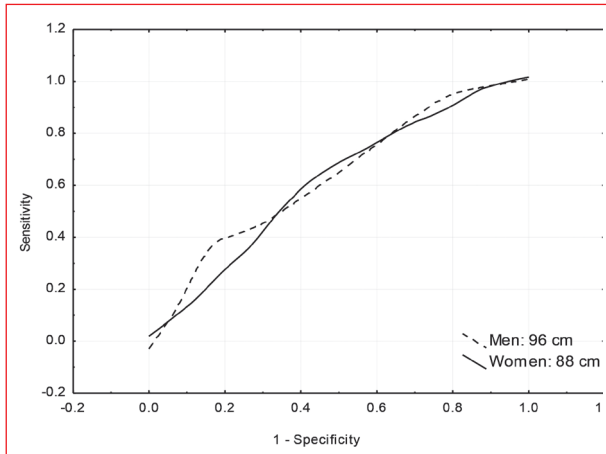
The area under the curve was 0.63 (95% confidence interval: 0.52-0.75) for the men and 0.61 (95% confidence interval: 0.47-0.76) for the women

Figure 1: Receiver operating characteristic curves depicting the waist circumference cut-off points for metabolic syndrome in Caucasian men and women

The area under the curve was 0.63 (95% confidence interval: 0.52-0.75) for the men and 0.61 (95% confidence interval: 0.47-0.76) for the women

Considering the cohort-specific WC cut-off, metabolic risk was suggested in men regarding their mean WC (106 cm), while women were just below the newly developed threshold, with a mean WC of 87 cm. To determine metabolic syndrome prevalence, we used both the JIS-recommended WC cut-offs, as well as the cohort-specific WC cut-off points.

Using the cohort-specific WC cut-off points, one less man and three less women presented with metabolic syndrome compared to the prevalence when the JIS cut-off points were used (Table II). Thus, metabolic syndrome prevalence remained similar using either the JIS, or cohort-specific, WC cut-off points, regardless of the difference in WC cut-off points between the JIS (80 cm) or the cohort-specific (88 cm) criteria, especially in women. The prevalence of high WC changed considerably when the new cohort-specific criteria were used in women, although metabolic syndrome prevalence remained nearly unchanged.

When using the JIS criteria, there was a 64% prevalence of the women having a high WC, but a prevalence of only 39% when using the WC cut-offs specific to this cohort. On further investigation, it was demonstrated that although 48% of the men and 30% of women had WC cut-off points above the cohort-specific WC, they did not present with metabolic syndrome. Only 33% and 8% of the men and women, respectively, with a WC above the cohort-specific cut-off point presented with metabolic syndrome. Thus, it seems that the definition of WC did not greatly affect the prevalence of metabolic syndrome in this specific Caucasian cohort, and that underlying cardiometabolic risk factors, other than WC, may have affected metabolic syndrome prevalence.

In order to determine which risk factors were more prone to contribute to metabolic syndrome prevalence, the AUC values were determined for each of the components of metabolic syndrome. Table III shows

**Table II:** The prevalence of high waist circumference and metabolic syndrome

	Men (n = 90)		Women (n = 96)	
	JIS/IDF WC (94 cm)	ROC WC (96 cm)	JIS/IDF WC (80 cm)	ROC WC (84 cm)
Metabolic syndrome prevalence, n (%)	31 (34.4)	30 (33.3)	12 (12.5)	9 (9.4)
High WC prevalence, n (%)	79 (87.8)	73 (81.1)	61 (63.5)	37 (38.5)
WC above the cut-off point, but no metabolic syndrome, n (%)	48 (53.3)	43 (47.8)	50 (52.1)	29 (30.2)
WC above the cut-off point and metabolic syndrome, n (%)	31 (34.4)	30 (33.3)	11 (11.5)	8 (8.3)

JIS/IDF: Joint Interim Statement/International Diabetes Federation, WC: waist circumference, ROC: receiver operating characteristic

Table III: The ranking of the metabolic syndrome risk factors according to area under the curve values

Men		Women	
Risk factor	AUC (95% CI)	Risk factor	AUC (95% CI)
Systolic blood pressure	0.84 (0.75-0.92)	Diastolic blood pressure	0.89 (0.82-0.96)
Diastolic blood pressure	0.78 (0.69-0.88)	Systolic blood pressure	0.84 (0.75-0.93)
Triglycerides	0.73 (0.64-0.85)	Glucose	0.83 (0.67-0.98)
Glucose	0.68 (0.56-0.81)	Neck circumference	0.80 (0.65-0.96)
Waist circumference	0.68 (0.57-0.79)	Waist circumference	0.77 (0.646-0.90)
Neck circumference	0.66 (0.54-0.78)	Triglycerides	0.74 (0.55-0.93)
High-density lipoprotein	0.53 (0.38-0.68)	High-density lipoprotein	0.48 (0.23-0.72)

AUC: area under the curve, CI: confidence interval
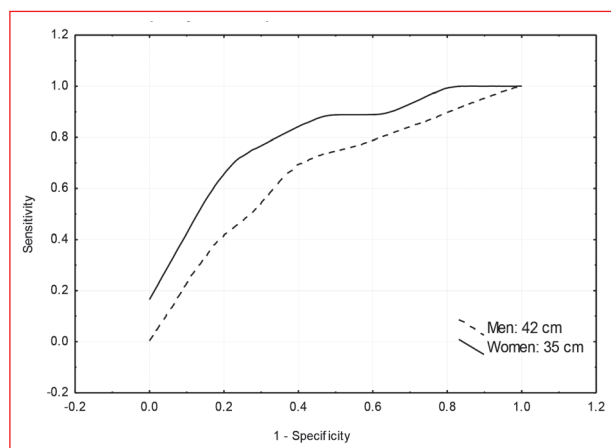
The area under the curve was 0.66 (95% confidence interval: 0.54-0.78) for the men and 0.80 (95% confidence interval: 0.65-0.96) for the women

Figure 2: Receiver operating characteristic curves depicting the neck circumference cut-off points for metabolic syndrome in Caucasian men and women

the AUC results. The contributing factors are presenting in descending order, from the highest to the lowest.

According to the AUC values, WC was a low contributor to metabolic syndrome, for the both men and women. Because metabolic syndrome is defined as the presence of three risk factors, we evaluated the top three components according to their AUC values. Blood pressure contributed greatly to the development of metabolic syndrome in both the men and women. Triglycerides and glucose were the third highest contributing factor in the men and women, respectively. The finding that NC was ranked higher than WC with respect to women was of interest. This could indicate that NC is a superior measure to WC when determining metabolic syndrome in women, especially considering the great variability in the WC cut-off points for women. The NC cut-off points determined for metabolic syndrome were 42 cm (AUC 0.66, 95% CI: 0.54-0.78) for men, and 35 cm (AUC 0.80, 95% CI: 0.65-0.96) for women (Figure 2).

The area under the curve was 0.66 (95% confidence interval: 0.54-0.78) for the men and 0.80 (95% confidence interval: 0.65-0.96) for the women.

Table IV: The prevalence of high waist circumference and hyptertension

	Men (n = 90)	Women (n = 96)
	ROC WC (96 cm)	ROC WC (84 cm)
Hypertension prevalence, n (%)	56 (62.2)	30 (31.3)
High WC prevalence, n (%)	73 (81.1)	37 (38.5)
WC above the cut-off point, but no hypertension, n (%)	25 (27.8)	18 (18.8)
WC above the cut-off point and hypertension, n (%)	48 (53.3)	19 (19.8)
WC above the cut-off point in hypertensive persons (men, n = 56; women, n = 30)	48 (85.7)	19 (63.3)

ROC: receiver operating characteristic, WC: waist circumference

As hypertensive status contributed more to metabolic syndrome prevalence than WC, we determined what the prevalence of hypertension and high WC were when using the WC cut-off points for metabolic syndrome (Table IV). 53.3% of the men and 85.7% of the men with hypertension presented with a WC above the cohort-specific cut-off point, whereas 19.8% of the women and 63.3% of the women with hypertension also presented with an increased WC.

Discussion

We demonstrated that the WC cut-off specific to our Caucasian cohort varied from the suggested Europid (JIS) cut-off points and that these cohort-specific cut-off points corresponded to the baseline findings.

Concerning the WC cut-off point for men, the cohort-specific WC cut-off point of 96 cm was similar to the JIS WC cut-off point of 94 cm, whereas the women's WC cut-off point of 88 cm varied greatly from the JIS cut-off point of 80 cm, in being a marker of metabolic syndrome. The same tendency, whereby men had a similar, and women a different, cut-off point than the JIS, was also found in black African men and women from the same area (WC cut-off point of 92 cm for men, and 94 cm for women).[15]

Referring to the WC cut-off points developed in the same group at baseline (in 2009), the men had a similar WC cut-off point (97 cm in 2009 and 96 cm in 2012), whereas there was a slight difference between the WC cut-off point of 84 cm at baseline[4] and 88 cm at follow-up for the women. This increase in the cut-off point may be ascribed to ageing or menopause, when women tend to develop a more android build, with an accompanying increase in visceral fat.[16] This is supported by the mean oestradiol value of the total female group, which was well above 32.2 pg/ml.[16] Approximately 29% of the women used hormone replacement therapy which could have further increased the higher oestradiol, and subsequently the WC, values.

When substituting the WC JIS cut-off points with the cohort-specific WC cut-off points in determining metabolic syndrome, it was assumed that metabolic syndrome prevalence would change or differ with the use of varying cut-off points. However, this was not the case. Metabolic syndrome prevalence was similar in both the men and women, regardless of which cut-off points were used. This could indicate that WC did not play a large role in determining metabolic syndrome outcome in the Caucasians in this cohort, and that other underlying cardiometabolic risk factors, other than WC, may have affected metabolic syndrome prevalence.

Furthermore, it was revealed that although women had a high WC (whether using the JIS- or the cohort-specific cut-off points), they do not necessarily present with metabolic syndrome, which could possibly be explained by the fact that their mean WC was below that of the cohort-specific WC.

Study highlights

Prevalence of metabolic syndrome prevalence did not change when we used the WC cut-off point that was specific to our cohort. Therefore, we wanted to determine which other factors affected metabolic syndrome prevalence more profoundly than WC. It was found that blood pressure affected metabolic syndrome prevalence the most in both the men and women in this cohort. Another finding from this study was that most men who had a high WC also presented with hypertension. Although blood pressure was the strongest contributor to metabolic syndrome prevalence in our study, more research is needed on sub-Saharan Caucasians with regard to blood pressure and hypertensive status. A general health survey of more than 59 000 individuals reported that hypertension was under-diagnosed, thereby increasing the significant burden of cardiovascular disease in South Africa.[17] The prevalence of high blood pressure in the mentioned population seems to have been underestimated. During this survey, the weighted prevalence of self-reported diagnosis of hypertension by a health professional was 10.4% in white South Africans, and the age-standardised rate was not significantly different by sex.[17] In our group, hypertension was under-diagnosed as well (15-38%), which may implicate the risk of future cardiovascular events. A national registry is urgently needed to inform the medical community of the prevalence of hypertension, cardiovascular events and survival estimates. This may impact on the medical treatment regime for metabolic syndrome and the approach for future cardiometabolic research.

Even though WC did not greatly affect metabolic syndrome prevalence in this cohort, it is still necessary to develop cut-off points that are specific to a particular group. WC or NC can easily be incorporated in any primary healthcare procedure. Despite anthropometric measures that were above the cut-off points which did not necessarily reflect metabolic syndrome prevalence in this cohort, having a value above a certain cut-off point could prompt healthcare action, which, in turn, could help to improve health.[8] Developing consistent WC values is a challenge in Caucasian women, although these women do not seem to be as vulnerable to metabolic syndrome as their male counterparts.

According to recent findings, it seems as if NC might be valuable to consider as an additive or alternative measure with which to ascertain the presence of metabolic syndrome. Present findings indicate that NC is ranked higher than WC as a contributor to metabolic syndrome prevalence (Table III), mostly in women. Prior baseline findings (40 cm for young and 41 cm for older Caucasian men; 34 cm for young and 33 cm for older Caucasian women),[11] were that the NC cut-off points for both the men and women remained similar to the present findings (42 cm for men and 35 cm for women). This finding could lead us to believe that over time, NC is more constant than WC in identifying metabolic syndrome prevalence, especially in women. It is already known that NC is an ideal measure because it does not change during the day or with menopausal status, as is the case with WC.[9] Therefore, it would seem that NC was a valuable anthropometric screening tool for metabolic syndrome for the women in this cohort, which confirms the findings from baseline.[11]

Indeed, increases in NC have been associated with cardiometabolic risk, as well as obstructive sleep apnoea (OSA).[18,19] A NC greater than 40 cm in women and 42.5 cm in men correlates with an increased risk of OSA, whereas increasing NC correlates with increased severity of OSA.[18] OSA, characterised by recurrent episodes of partial or complete upper airway obstruction during sleep, has been newly recognised as a secondary cause of hypertension. We evaluated OSA via the validated Berlin questionnaire,[20] where the prevalence of OSA was evident in 30.65% of the Caucasian cohort. OSA triggers a cascade of adverse effects, including increased sympathetic activity, systemic inflammation and metabolic dysregulation that may contribute to poor blood pressure control.[19] The poor blood pressure control in our population exemplifies the importance of screening for OSA and NC to evaluate cardiometabolic function.

Strengths and limitations of the study

A strength of this study was the inclusion of a unique, homogenous group of urban Caucasians from North West province within a highly standardised experimental protocol. A further strength was that we contributed to novel data on ethnic-specific anthropometric cut-off points. The study was limited by the sample size as we could only include participants from the baseline study. Additionally, because of the specific characteristics of the participants (region, occupation and income), the results cannot be applied to other Caucasian populations in Africa. Therefore, larger sample sizes in more diverse groups should be assessed in order to obtain more valid and clinically applicable recommendations.

Conclusion

We conclude that cohort-specific WC cut-off points differ from the JIS cut-off points and that the WC and NC cut-off points from the present study strengthened the cut-off points from baseline, especially in men. We cautiously suggest that as an identifier of metabolic syndrome, the WC cut-off points should be 96 cm and 88 cm for the men and women, respectively, in this cohort. We also found that the NC cut-off points for metabolic syndrome were 41 cm and 35 cm for the men and women, respectively, in this Caucasian cohort. From a clinical perspective, we recommend applying NC, rather than WC, as an anthropometric measure of metabolic syndrome in women as it was a stronger predictor thereof, and may not be influenced by menopausal status *per se*.

Acknowledgements

Conflict of interest

The authors declare that no conflict of interest existed which may have inappropriately influenced them when writing this paper.

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