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From the Editor's Desk

This issue examines mainly cardiovascular disease risk factors in Africa. Macia and colleagues studied obesity in Senegal, with a focus on rural versus urban trends (page 74). One of the consequences of urbanisation in developing countries is increasing rates of obesity and its adverse sequelae, as seen in Nigeria as well.[1] Subgroups of the population, such as young women, have high rates of obesity in both urban and rural settings and this needs to be investigated further and dealt with.

Onen also shows high obesity rates in Botswana and, worryingly, the metabolic syndrome correlates are also high (page 44). While Botswana's economy is doing well,[2] consequences such as reduced reliance on traditional diets[3] may be leading to adverse health effects, such as obesity.

Kingue *et al.* examined the metabolic syndrome correlates for coronary artery disease in areas in sub-Saharan Africa (Cameroon, Madagascar, Nigeria and Democratic Republic of Congo) and also show high levels of these risk factors (page 50). The implication is that many countries in Africa are sitting on a time bomb of non-communicable diseases, in addition to the traditional communicable disease burden that they already have.[4] Is it time to look more extensively at interventional policies on a local, regional or even continental scale?

Furat and co-workers, in a study in Istanbul, Turkey, looked at the beneficial effect of telmisartan in reducing microalbuminuria after coronary artery bypass grafting in patients with diabetes (page 57). This is compatible with the known beneficial effects of angiotensin receptor blockers.[5]

Celik *et al.* researched red cell distribution values (RDW) as a correlate of extensive coronary heart disease in diabetes (page 61). It is a readily available and cheap test and may help with clinical decisions in low-resource settings. RDW has been linked to adverse outcomes in patients with coronary artery disease, heart failure and stroke.[6,7] One of the issues with RDW is whether its measurement is standardised enough to be of use,[8] and another is whether it contributes materially to clinical assessment.[9] Its role is still unclear.

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S Afr J Diabetes Vasc Dis 2017; **14**: 43

Obesity in Botswana: time for new cut-off points for abdominal girth?

CHURCHILL LUKWIYA ONEN

Abstract

Introduction: **Country-specific cut-off points for defining central obesity in black Africans are long overdue.**
Methods: **Anthropometric data from 215 (51.4%) male and 203 (48.6%) female patients seen in Gaborone between 2005 and 2015 were analysed to establish appropriate cut-off points for waist circumference (WC) corresponding to a body mass index (BMI) of 30 kg/m². Relative risks for cardiometabolic disorders were calculated for different BMI and WC categories using MedCalc®. The subjects' mean age was 50.0 ± 10.8 years and 80.6% were Batswana.**
Results: **Only 7.2% of patients had a BMI < 25 kg/m², 27.3% were overweight and 65.5% were obese; mean BMI was 34.9 ± 6.5 kg/m² in the women versus 31.0 ± 4.9 kg/m² in the men ($p < 0.0001$). New cut-off points of 98 cm in men and 85 cm in women emerged. Different weight and WC categories appeared not to confer increased relative risk of hypertension, dysglycaemia or dyslipidaemia.**
Conclusion: **The proposed WC cut-off values, if validated, should set the pace for larger studies across sub-Saharan Africa.**

Keywords: Botswana, obesity, waist circumference, cut-off points, modelling

Several small observational studies in Botswana have produced inconsistencies in the prevalence of the metabolic syndrome (MetS), partly because of variations in methodological approaches to measurements of waist circumference and differences in study populations.[1-3] Although Botswana was one of the poorest countries at independence, its diamond-dependent economy has propelled it to upper-middle income, with one of the fastest-growing economies in the world, gross domestic product of $18 825 per capita in 2015, the fourth largest gross national income, and the highest human development index in sub-Saharan Africa.[4,5]

It is currently estimated that 57% of the population is urbanised. Overweight and obesity are therefore assuming epidemic proportions in the country. Life expectancy at birth is 63 and 65 years in men and women, respectively.[6,7] This represents a 14-year increase for both genders between 2000 and 2012. The probability of dying between the ages of 15 and 60 years in men and women is 321 and 254 per thousand of the population, respectively.

In 2012, HIV/AIDS accounted for a third of the causes of mortality (5 700 deaths), whereas stroke, ischaemic heart disease, diabetes mellitus and hypertensive heart disease together accounted for about 15% of deaths (2 900 deaths). Cardiovascular diseases and diabetes together constituted the third most common cause of disability-adjusted life years (DALYs).

Since its description by Jean Vague[8] nearly seven decades ago, abdominal obesity consistently features among criteria for the definition of the MetS, although the clustering of cardiovascular risk factors has greatly expanded. Obesity is also the bedrock in the International Diabetes Federation (IDF) definition of the MetS.[9] The Joint Interim Statement (JIS) on the MetS recommended the use of population- and country-specific cut-off points to define an enlarged waist circumference.[10] Accordingly, using non-validated cut-off points for waist circumference in the definition of obesity may falsify estimates of the MetS in the African setting. Inconsistent estimates of the MetS in sub-Saharan Africa have largely been due to lack of African-specific cut-off points for waist circumference.[11-13]

This study aimed firstly to determine the validity of current operational waist circumference cut-off points in Botswana; secondly, to determine the correlation between body mass index (BMI) and waist circumference (WC) in black African men and women, and in particular, the relationship between BMI of 30 kg/m² and WC of 80 cm in women and 94 cm in men; and thirdly whether excessive body weight relates to cardiometabolic and other chronic medical disorders in the study population.

Methods

Data from a heterogeneous group of adult patients seen over a 10-year period (2005–2015) at a specialised medical clinic I run in Gaborone city were extracted from conveniently sampled case notes, taking every sixth file from over 3 000 files accumulated in the filing room during a decade of private practice. Completeness of records was examined for the presence of weight (kg), height (cm), waist circumference (cm) and co-morbidities for each patient during the index visit.

From the inception of the clinic at Gaborone Private Hospital, anthropometric measurements have been routinely performed whenever possible, using standard methods. Weight (kg) and height (cm) were measured in a similar manner to the method described by Dowse and Zimmet,[14] using a well-calibrated scale. BMI was derived by dividing weight (kg) by the square of height (m²). Able-bodied participants were instructed to stand upright with the back against the stand, heels together and eyes directed forward so that the top of the tragus of the ear was horizontal with the inferior orbital margin, and the measuring plate was lowered on to the scalp to give the correct height.

Waist circumference was measured with the individual standing upright with the side turned to the observer, who was often seated. A measuring tape attached to a spring, similar to that used in the INTERHEART study,[15] was placed snugly in a horizontal plane around

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the subject's abdomen, mid-way between the rib cage and the iliac crest, and standard tension was applied.

Demographic data, anthropometric measurements and co-morbidities for individual patients were entered into a database created using the Statistical Package for Social Sciences (IBM SPSS statistics 20®). Correlation plots were made for BMI (kg/m²) and WC (cm) in men and women, using 30 kg/m² as the reference cut-off point for obesity, to determine corresponding mean WC (+ 95% CI) in both genders. Similar plots were made for BMI and WC using 94 cm in men and 80 cm in women as reference cut-off points for obesity to determine corresponding BMI (+ 95% CI) in both genders. Height (m) was also plotted against WC in both men and women.

Patients were grouped into five WHO weight categories:[16] normal weight (category 1; BMI 18.5–24.9 kg/m²), overweight (category 2; BMI 25.1–29.9 kg/m²), grade I obesity (category 3; BMI 30.0–34.9 kg/m²), grade II obesity (category 4; BMI 35.0–39.9 kg/m²), and grade III obesity (category 5; BMI ≥ 40.0 kg/m²). Women were arbitrarily grouped into three WC categories: category 1 (WC ≤ 80 cm), category 2 (WC 80.0–87.9 cm) and category 3 (WC ≥ 88 cm). Men were likewise grouped into three WC categories: category 1 (WC ≤ 94 cm), category 2 (WC 94.0–101.9 cm) and category 3 (WC ≥ 102 cm).

Statistical analyses

With MedCalc® software,[17] using category 1 BMI and category 1 WC as references, relative risks (+ 95% CI) for hypertension, dysglycaemia and dyslipidaemia were calculated for different BMI and WC categories. Sample means and standard deviations were calculated in the conventional way. Level of statistical significance was taken to be $p < 0.05$.

Results

A total of 498 case notes were retrieved; 23 did not contain the required data. Of 475 case notes of patients with the required anthropometric parameters, 20 naturalised non-black citizens of Botswana, 25 Asians and 12 Caucasians were excluded; the remaining 418 black African patients were analysed. This consisted of 215 men (51.4%) and 203 women (48.6%), mean age 50.0 ± 10.8 years, 80.6% of whom were Batswana and 19.4% were other black Africans.

Only 7.2% had normal weight (BMI 18.5–24.9 kg/m²), 27.3% were overweight (BMI 25–29.9 kg/m²) and 65.5% were obese (BMI > 30 kg/m²). Significantly more women were obese (77.8%) compared to men (54.0%); mean BMI was 34.9 ± 6.5 versus 31.0 ± 4.9 kg/m² ($p < 0.0001$). Hypertension affected 77.8% (325/418) and dysglycaemia 44.3% (185/418) of the patients. Lipid profiles were not estimated in a third of the sample group. Dyslipidaemia was documented in 67% of the remaining 279 patients.

One man did not have a WC measurement and was excluded from the correlation plots. WC directly correlated with BMI in both genders (R2 linear = 0.774 in men; 0.644 in women) with new cut-off points of 98 cm (95% CI: 96.9–98.2 cm) in men and 85 cm (95% CI: 83.0–86.5 cm) in women, corresponding to BMI of 30 kg/m². (Fig. 1A, B). The current operational WC of 94.0 cm in black African men corresponded to a BMI of 28.7 kg/m², whereas in black women, the corresponding BMI was 28.0 kg/m² for a WC of 80 cm (Fig. 2A, B).

In both men and women, there was a poor correlation between height and WC (R^2 linear = 0.036 in men; 0.005 in women) (Fig. 3A, 2B). There was no correlation between age and BMI among the 418 patients (R^2 linear = 0.001).

Table 1 shows the relative risks of hypertension, dysglycaemia and dyslipidaemia for different BMI categories versus normal weight (BMI < 25 kg/m²) among 418 patients. Table 2 shows the relative risks of any cardiovascular disease for different WC categories versus current reference WC (< 80 cm in women; < 94 cm in men). Both tables demonstrate no overall statistically significant risk relationship with hypertension, dysglycaemia and dyslipidaemia. Separate analysis showed that WC ≥ 102 cm in men was associated with 21% increased total co-morbidity, combining cardiometabolic and musculoskeletal disorders (RR 1.21; 95% CI: 1.03–1.42; $p = 0.022$).

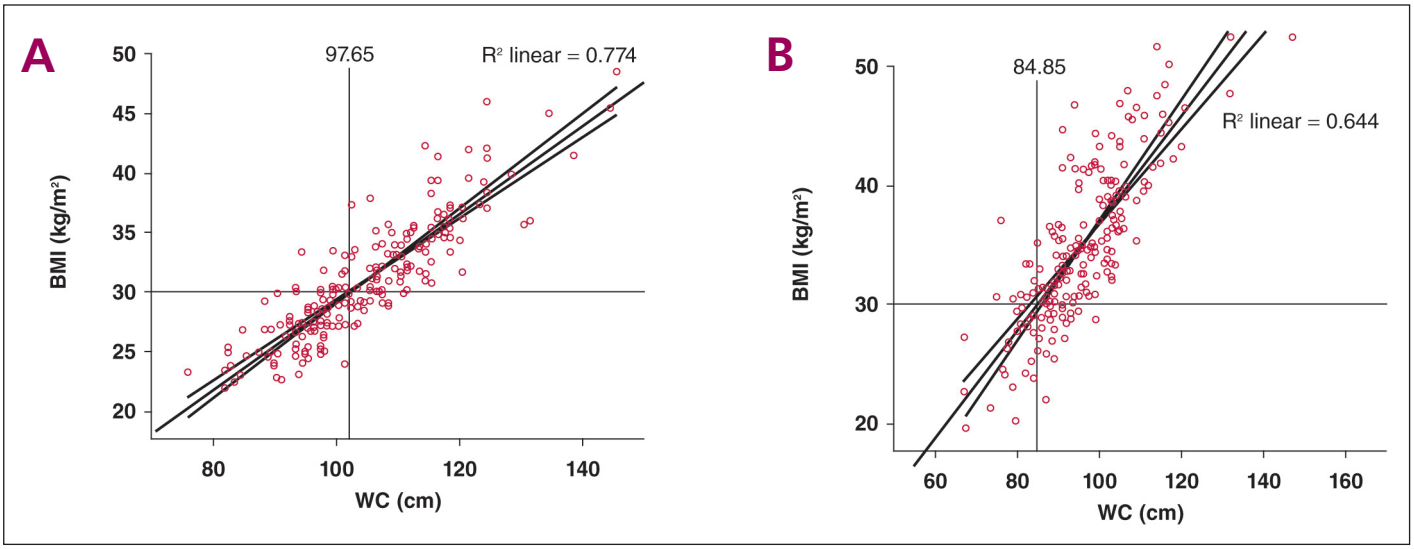

Figure 1. Correlation between BMI (kg/m²) and WC (cm) in (A) 214 men and (B) 203 women with BMI = 30 kg/m² as cut-off point. BMI, body mass index; WC, waist circumference.

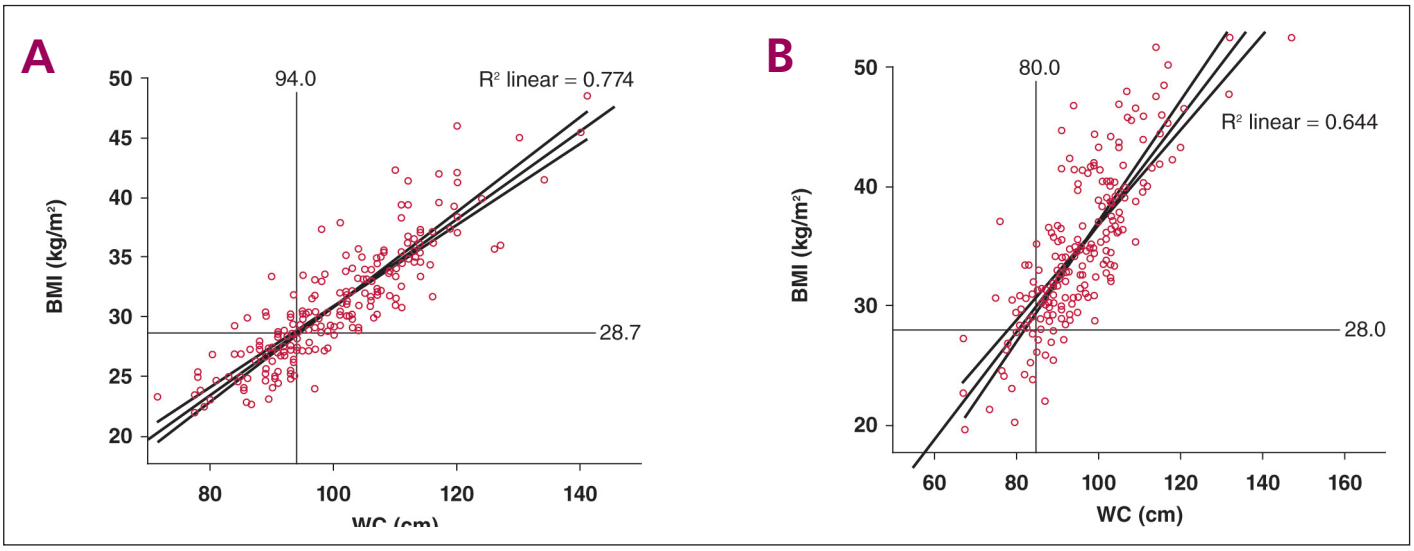

Figure 2. Correlation between BMI (kg/m²) and WC (cm) in (A) 214 men with WC = 94.0 cm and (B) 203 women with WC = 80 cm as cut-off point. BMI, body mass index; WC, waist circumference.

Discussion

There are strong indications for examining body size in the current context of affluence, social marketing and food consumption in Botswana. Anthropometric measurements are frequently used to determine parameters of overweight and obesity at most points in the healthcare system and during many 'wellness' programmes. Knowing that a person's BMI exceeds 30 kg/m² may be useful only in understanding the individual's potential cardiometabolic risk and total burden of co-morbidity. After all, obesity may be an epiphenomenon for other cardiovascular disease risk factors. But failure to recognise obesity as a major health issue and its complex social and societal construct may camouflage the problem and propagate inherent imperfections of the obesity-screening processes.

Cataloguing BMI, WC and sometimes waist:hip ratios may not reflect their correlation to obesity-related sequelae. There are medically healthy obese individuals and metabolically obese normal-weight individuals, although the prevalence of these conditions in this community is unknown. National anthropometric data are scarce or unavailable.

The growing prevalence of overweight and obesity sweeping southern Africa, with a national prevalence between 30 and 60% of populations over the age of 15 years, is largely due to dietary shift away from high-fibre, low-calorie diets rich in fruits and vegetables towards refined, energy-dense foods high in fat, calories, sweeteners and salt, and this affects females disproportionately.[18,19] A paradoxical situation, in which poverty and high levels of overweight and obesity co-exist in urban settings, may be explained by reduced levels of physical activity in all groups. Coupled with rapid urbanisation, industrialisation and increased sedentary lifestyles, these nutritional and demographic transitions have ushered in the rapid emergence of non-communicable diseases, including hypertension, diabetes, stroke, heart disease and other cardiovascular diseases.

Despite direct correlations between BMI and WC, findings from this situational analysis in Botswana suggest the need for new cut-

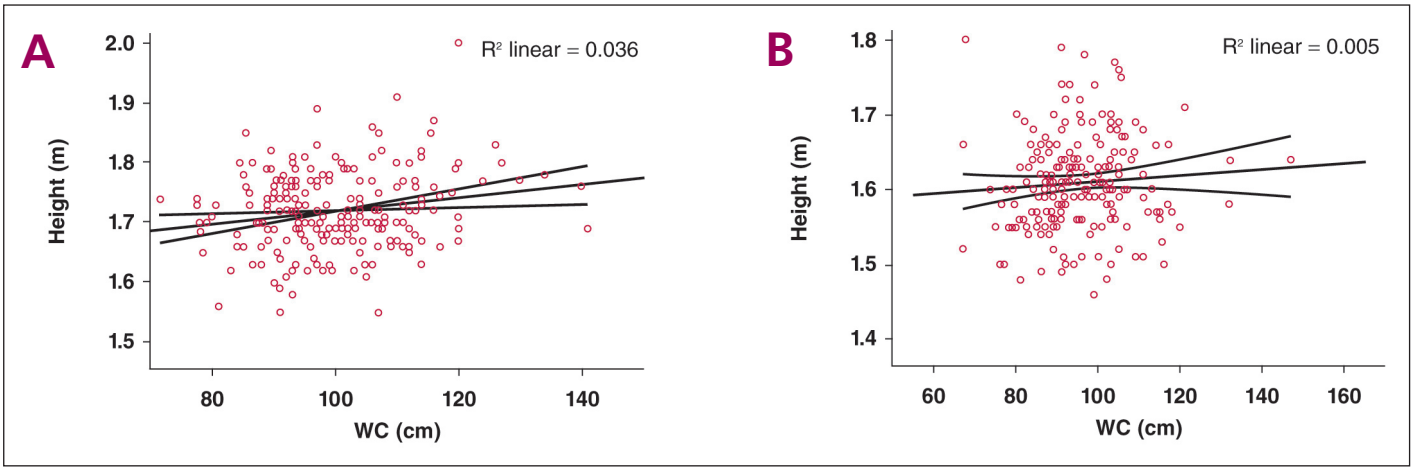

Figure 3. Poor correlation between height and WC in (A) 214 men and (B) 203 women. WC, waist circumference.

Table 1. Relative risks of hypertension, dysglycaemia and dyslipidaemia for different BMI categories versus normal weight (BMI < 25 kg/m²) among 418 patients

	(1) Hypertension, (2) dysglycaemia, (3) dyslipidaemia		
WHO BMI category (kg/m²)	**Relative risk**	**95% CI**	***p*-value**
Overweight (25–29.9)	(1) 0.99	(0.78–1.27)	0.95
	(2) 0.94	(0.61–1.45)	0.78
	(3) 1.24	(0.79–1.96)	0.36
Grade I (30–34.9)	(1) 1.09	(0.87–1.38)	0.45
	(2) 0.88	(0.57–1.36)	0.57
	(3) 1.24	(0.79–1.95)	0.36
Grade II (35–39.9)	(1) 1.12	(0.88–1.43)	0.45
	(2) 1.01	(0.65–1.59)	0.95
	(3) 1.07	(0.66–1.74)	0.77
Grade III (> 40)	(1) 1.06	(0.82–1.38)	0.64
	(2) 1.02	(0.64–1.62)	0.94
	(3) 1.23	(0.76–1.98)	0.40

WHO, World Health Organisation; BMI, body mass index.

Table 2. Relative risks of any cardiovascular disease for different waist circumference categories versus current reference waist circumferences (< 80 cm in women; < 94 cm in men)

	Any CVD relative risk		
Waist circumference category (cm)	**Relative risk**	**95% CI**	***p*-value**
Category 2			
Men (94–101.9)	1.04	(0.91–1.18)	0.61
Women (80–87.9)	1.15	(0.84–1.59)	0.39
Category 3			
Men (> 102)	1.10	(0.99–1.22)	0.08
Women (> 88)	1.17	(0.86–1.58)	0.32

CVD, cardiovascular disease refers to hypertension, dysglycaemia and dyslipidaemia.

off points for WC (98 cm in men; 85 cm in women) that correspond to a BMI of 30 kg/m². Europid WC cut-off points (≥ 80 cm in women; ≥ 94 cm in men), as recommended by the IDF[9] and currently used in sub-Saharan Africa to define central obesity do not appear to correlate with BMI ≥ 30 kg/m² in Botswana. Elsewhere, there is a strong correlation between BMI of 25–34.9 kg/m², WC ≥ 102 cm for men and ≥ 88 cm for women, and greater risk of hypertension, type 2 diabetes, dyslipidaemia and coronary heart disease.[20]

Western countries derived cut-off values of WC from correlation with BMI, whereas Asians tried to define WC cut-off values produced by receiver-operating characteristics (ROC) curve analysis.[21,22] Measurements of skinfold thickness are less accurate, particularly in obese individuals and are therefore discouraged in routine screening exercises, except in epidemiological studies. Precise measurements of body fat using computed tomography (CT) or magnetic resonance imaging (MRI) scans or biochemical barometers such as adipokines are unlikely to be used outside research settings in Botswana. However, measurement of fasting insulin and glucose levels may help in the calculation of HOMA-IR in individuals with features of insulin resistance syndromes.

In the Diabetes and Macrovascular Complications study of 258 adult diabetic patients in Botswana,[1] the MetS defined using IDF criteria[9] was more prevalent in diabetic women compared to diabetic men. Depending on which set of parameters in the IDF criteria was used for the definition, the prevalence of the MetS ranged from 41.7–83.7% in men, and 37.8–88.6% in women. Obesity, defined by waist:hip ratio (> 0.9 in men, > 0.85 in women) was present in 87.9% of diabetics, and by WC (> 94 cm men, > 80 cm in women) in 79.0% of diabetics, but prevalence of the MetS dropped to 38.3% using BMI (> 30 kg/m²). Large disparities in estimates of the MetS based on different parameters complicated its true prevalence estimates in that study. BMI was viewed as an insensitive indicator of the MetS, especially in diabetic women.

Garrido *et al.*[2] conducted a small cross-sectional, observational study of 150 hospital workers at a peripheral facility in Botswana, representing nearly half of the hospital workforce, women comprising over 70% of the group. The investigators applied any three or more of the ATP III criteria for definition of the MetS.[23] Low high-density lipoprotein (HDL) cholesterol affected 80% of the group, dysglycaemia 73.3%, hypertension 44%, central obesity 42% and hypertriglyceridaemia 14%. A third of the participants met the ATP III criteria for the MetS and 28.7% had a BMI > 30 kg/m². That over 40% of hospital employees had central obesity, using higher cut-off points for WC raises the possibility of a high prevalence of abdominal obesity in the community.

Another cross-sectional study by Malangu[3] looked at 190 adult HIV-infected patients on highly active antiretroviral therapy (HAART) at Princess Marina Hospital in Gaborone in 2010. Their mean age was 42 ± 9.04 years and nearly threequarters of the group were women (74.2%). Using IDF criteria, the investigator showed an overall prevalence of the MetS in 11.1% of participants. Risk factors for the MetS included increased age, male gender

and longer exposure to antiretroviral drugs, particularly protease inhibitors. Only 10% of participants had a BMI > 30 kg/m^2, 13 of 141 women and eight of 49 men had abdominal obesity (WC ≥ 80 cm in women and ≥ 94 cm in men).

The study design lacked comparator control groups (e.g. non-HIV-infected individuals or HIV-infected persons pre-HAART), making it difficult to determine the independent contribution of antiretroviral therapy to the MetS and this limits generalisability of the findings. However, it appears that obesity and the MetS were substantially lower in HIV-infected individuals, despite the use of different diagnostic criteria for the MetS.

Studies from other parts of sub-Saharan Africa have generated wide variations in WC cut-off points. For example, central obesity defined by WC > 102 cm in men and > 88 cm in women was more common than generalised obesity (BMI > 30 kg/m^2) in Cotonou, Benin.[11] In South Africa, Motala et al.12 found that WC of > 86 cm in men and > 92 cm in women predicted the presence of at least two elements of the MetS in a cross-sectional, population-based study in a rural setting. That study was heavily gender biased, with 80% of the 947 participants being female.

In 2014 Magalhães *et al.*,[13] in another cross-sectional study of 615 university employees in Luanda, Angola, found overall prevalence of overweight to be 47.8%, and obesity in 45.2% of participants. Using JIS criteria, crude and age-standardised prevalence of the MetS were 27.8 and 14.1%, respectively. The crude and age-standardised prevalence of the MetS was 17.6 and 8.7% using ATP III criteria,[23] which apply higher WC cut-off points (≥ 102 cm in men, ≥ 88 cm in women).

Applying ROC curves of WC to detect the MetS, new cut-off points of this study were 87.5 cm in men (sensitivity 75.9%, specificity 81.2%) and 80.5 cm in women (sensitivity 88.4%, specificity 60.5%). The three most common criteria for the MetS were increased WC, hypertension and low serum HDL cholesterol levels. Women showed a higher prevalence in all age groups from the age of 30 years.

The INTERHEART study, a case-controlled study of 27 000 participants from 52 countries, showed a graded and highly significant association between waist:hip ratios (WHR) and acute myocardial infarction worldwide.[15] The association of WHR with acute myocardial infarction in the INTERHEART study addressed one of the most fundamental cardiovascular sequelae of excessive and disproportionate weight. Although the INTERHEART study investigators cast doubt on the use of BMI in the context of acute myocardial infarction, obesity, however defined, was associated with a myriad of conditions, including hypertension, diabetes mellitus, dyslipidaemia, obstructive sleep apnoea, gastro-oesophageal reflux, sudden death, stroke, certain types of cancer, infertility, degenerative joint disease and negative psychosocial impact.

The Prospective Studies Collaboration addressed the association of BMI with cause-specific mortality in about 900 000 adults in 57 prospective studies.[24] These authors concluded that other anthropometric measures such as WC and WHR could well add extra information to BMI, and BMI to them, but that BMI is in itself a strong predictor of overall mortality rate both above and below the apparent optimum of about 22.5 to 25 kg/m^2.

For screening purposes, it appears that measurements of WHR provide no advantage over WC alone, are cumbersome and may be fraught with errors in field situations. Furthermore, it may not be necessary to measure WC in persons with BMI > 35 kg/m^2 since it adds little value in the predictive power of disease-risk classification.[25] Inconsistencies in cut-off values for WC have potentially undesirable consequences for cardiovascular risk stratification, disease categorisation and prioritisation of preventative strategies for obesity. There is therefore a strong need for validation of these WC cut-off values for Botswana before they can be used for prediction of incident outcomes such as cardiovascular diseases or type 2 diabetes mellitus.

Modelling may help to capture the scope and complexity of the obesity problem in Botswana. Applications of heterogeneous adaptive pieces of the puzzle that are affected by and/or influence the overall behaviour of individuals within society may lead to the development of empirically based public health models. Agent-based modelling (ABM) represents one such simplified example.[26] Using the ABM approach, agents could represent individuals, their attributes, behaviours and relationships with other individuals in society. The environment could represent geographical locations, mobility, domestic settings, market forces and social networking.

Systematic dynamic modelling (SDM) or perhaps more appropriately for Botswana, the MicroSimulation model, could be used to establish temporal and causal associations, if any, between obesity and related disorders, such as hypertension, diabetes, abnormal lipids, cardiovascular diseases, cancers, degenerative musculoskeletal disorders and psychological afflictions.[27] The strategy focuses on 'upstream' preventive approaches rather than 'downstream' acute and chronic care. The goal is to enhance the number of safer, healthier people and prevent others from becoming vulnerable or being afflicted by obesity and its related complications.

There are, however, several limitations of this study worth mentioning. Firstly, this was a retrospective analysis of case notes of a small number of patients seen at a specialised private medical practice. The finding may not therefore apply to the general population. Secondly, WC reflects both subcutaneous and visceral fat and at best represents a crude surrogate for visceral adiposity. Because women generally have more subcutaneous fat, there is a potential risk of misclassifying them as viscerally obese, thereby resulting in overestimation of the MetS in women. Thirdly, little is known about the full impact of the obesity epidemic on the health of the community, and failure to demonstrate statistically significant links between obesity and existing co-morbidities in this study should not be construed to suggest benignness of obesity in this population.

Conclusion

This study reiterates the need for ethnic-specific WC cut-off points for defining central obesity and, by extension, for diagnosis of the MetS among black Africans. The proposed WC cut-off values, if validated, will set the pace for larger studies across sub-Saharan Africa. Variations in WC cut-off values illustrate the uniqueness of populations.

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What two minutes a week of high-intensity exercise can do

Researchers from Abertay University report that high-intensity training (HIT) of short duration not only reduces the risk of disease, but is also just as effective at doing so as the exercise guidelines currently recommended, according to a study by Simon Adamson and colleagues published in *Biology* 2014; **3**(2): 333–344.

Current guidelines state that five 30-minute sessions of exercise should be carried out each week, something that very few people manage to achieve. The most common reason cited for this is lack of time, and the researchers believe that HIT is the perfect way for people who are time-poor to improve their health.

In the study, overweight adults took part in a HIT programme for a period of eight weeks. This involved completing twice-weekly sprint series on an exercise bike, with each sprint lasting just six seconds. Ten sprints were completed in total during each session, amounting to just two minutes of exercise per week.

This short HIT programme was enough to significantly improve cardiovascular health and insulin sensitivity in the participants, and is the first time that so little exercise has been shown to have such significant health benefits. Previous research by the same team had shown that three HIT sessions a week were required, but this study has eclipsed these results by showing that the same results can be achieved with just two.

Dr John Babraj, head of the HIT research team at Abertay University, explains: 'With this study, we investigated the benefits of HIT in a population group known to be at risk of developing diabetes: overweight, middle-aged adults.

'We found that not only does HIT reduce the risk of their developing the disease, but also that the regimen needs to be performed only twice a week in order for them to reap the benefits. And you don't have to be able to go at the speed of Usain Bolt when you're sprinting. As long as you are putting your maximal effort into the sprints, it will improve your health.

'And this is the beauty of HIT: it is quick to do and it is effective. Although it is well-established that exercise is a powerful therapy for the treatment and prevention of type 2 diabetes, only 40% of men and 28% of women achieve the recommended 30 minutes of moderate-intensity exercise on five days of the week.

'Lack of time to exercise, due to work or family commitments, is cited as the most common barrier to participation, so HIT offers a really effective solution to this problem and has the added benefit of reducing disease risk which activities such as walking, even if done five days a week for 30 minutes, don't offer.

'There is a clear relationship between the intensity of exercise and the magnitude of health improvement, so it is only through these short, high-intensity sprints that health improvements can be seen.'

Source:

http://www.diabetesincontrol.com/articles/diabetes-news/16355-what-two-minutes-a-week-of-high-intensity-exercise-can-do

Prevalence of selected cardiometabolic risk factors among adults in urban and semi-urban hospitals in four sub-Saharan African countries

SAMUEL KINGUE, SOLOFONIRINA RAKOTOARIMANANA, NIRINA RABEARIVONY, FRANCOIS LEPIRA BOMPERA

Abstract

Aim: **Cardiovascular diseases (CVDs) are a global challenge but the burden in sub-Saharan African (SSA) countries is less well documented than elsewhere. We aimed to describe the key cardiometabolic risk factors in four SSA countries.**

Methods: **A cross-sectional, multi-national, hospital-based study was carried out among adults (> 35 years) across four SSA countries from 12 December 2011 to 7 February 2013. Risk factors were defined using the World Health Organisation and International Diabetes Federation guidelines.**

Results: **Of the 844 adults (57.4% female, mean age 52.6 years), 76.6% were urban residents. The predominant CVD risk factors were hypertension (74.1%), obesity (36.2%) and excessive alcohol consumption (25.6%). Diabetes (17.7 vs 10.0%), obesity (42.8 vs 16.8%) and hypercholesterolaemia (25.8 vs 18.0%) were more prevalent among the hypertensive subjects (all $p < 0.007$) than the normotensives. The metabolic syndrome (39.4%) was more common in women and hypertensive subjects.**

Conclusions: **Hospital patients in SSA countries present with excessive rates of cardiometabolic risk factors. Focus on their prevention and control is warranted.**

Keywords: cardiovascular risk factors, metabolic syndrome, sub-Saharan Africa

Non-communicable diseases (NCDs) are rapidly increasing in incidence in sub-Saharan Africa (SSA). Cardiovascular disease (CVD) is the leading contributor to the global burden of NCDs.[1] Hypertension, which is the main driver of CVD, has been estimated to affect about 972 million adults worldwide, a figure that is projected to increase by 60% by the year 2025.[2,3] This high prevalence of hypertension is coupled with poor detection, treatment and control rates.[4]

Diabetes mellitus is also a leading cause of morbidity and mortality from NCDs and a major precursor of CVD.[5] The population of people with diabetes in SSA is growing more rapidly than anywhere else, and is expected to nearly double within the next two decades.[6] The co-occurrence of diabetes and hypertension in the same individual compounds the harmful effects of each condition.

A recent cross-sectional study conducted in semi-urban Cameroon has indicated the co-occurrence of diabetes and hypertension, affecting up to 5% of adults.[7] Other common drivers of NCDs and the CVD burden include physical inactivity, smoking, unhealthy diet, dyslipidaemia, excess weight and alcohol abuse.[8,9]

Monitoring the risk profile of the population is an extremely important component of the strategy to prevent and control NCDs in general and CVD in particular. This pivotal role was recently highlighted in the World Health Organisation (WHO) global action plan of 2013–2020 for the prevention of NCDs.[10] Given the silent nature of hypertension and other risk factors, and the lack of awareness of them in low- and middle-income countries (LMICs), opportunistic screening and awareness have been highlighted by the World Heart Federation as the key first steps to improving management and prevention.[11]

Studies addressing the risk profile of individuals who have contact with hospitals in Africa are lacking, and most of the existing studies are single-country studies, therefore offering less opportunity to examine between-country variabilities. This report is on a multi-country, multi-centre, health facilities-based study to assess the distribution of major cardiometabolic risk factors in adults in urban settings across different countries in SSA.

Methods

This was a multi-national, multi-centre, cross-sectional study conducted from 12 December 2011 to 7 February 2013. The following SSA countries participated in the study: Cameroon (13 centres), Nigeria (five centres), Democratic Republic of Congo (DRC) (11 centres) and Madagascar (24 centres). The study centres were purposefully selected from the health districts of the capital cities (urban and semi-urban) in the participating countries. Participating centres included both public and private healthcare facilities. General practitioners working in the selected centres were trained to consecutively recruit all individuals aged over 35 years to their facilities, regardless of the reason for the visit to hospital, if they were resident in the particular city for at least three months.

Ethical approval was obtained from the ethics committees of the participating countries and the patients gave written consent before

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enrollment. The study complied with the Declaration of Helsinki.

Data were collected simultaneously in all study centres of the participating countries, using a standardised case report form (CRF). The following variables were collected: socio-demographic characteristics (age, gender, educational level, alcohol consumption, tobacco use and employment type), history of hypertension, diabetes status and systolic and diastolic blood pressure (BP, in mmHg).

BP was measured using an automated BP machine (Omron 750 IT) in the seated position after the participant had been at rest for five to 10 minutes. Three measurements were taken on the right arm and the average of the last two was retained.[12] Weight, height, and waist and hip circumference were measured using standard procedures and equipment following WHO guidelines.[13] Weight was measured to the nearest 0.5 kg and height to the nearest 0.5 cm. Body mass index (BMI, kg/m^2) was calculated as body weight in kg divided by the square of the height in metres. The waist circumference (WC) was measured with a tape midway between the lower rib margin and iliac crest. Waist-to-hip ratio was calculated as waist circumference (cm) divided by hip circumference (cm).

Fasting capillary glucose concentration was obtained using a standardised glucometer (Accu-chek Aviva; Hoffmann-LA Roche, Ltd, Germany) in all the settings. Fasting total cholesterol, high-density lipoprotein (HDL-C) and low-density lipoprotein cholesterol (LDL-C), triglycerides, uric acid and serum creatinine concentrations were acquired using locally available routine standard techniques and procedures.

Hypertension was diagnosed in the presence of systolic or diastolic blood pressure ≥ 140 or 90 mmHg or ongoing blood pressure-lowering medications over the past 15 consecutive days. Uncontrolled hypertension was defined as blood pressure ≥ 140/90 mmHg in participants on BP control agents for the last 30 consecutive days. Duration of hypertension was defined as date of survey minus date of diagnosis of hypertension.

Hyperglycaemia was defined as fasting capillary glucose level ≥ 6.1 mmol/l (110 mg/l) and diabetes was defined as fasting capillary glucose level ≥ 7.1 mmol/l (126 mg/dl) or physician-documented history of diabetes, or patient on glucose-controlling agents (oral or insulin) for the last 15 consecutive days. Impaired fasting glycaemia was defined as fasting capillary glucose levels between 6.1 and 7.1 mmol/l (110–126 mg/dl).

Overweight and obesity were defined using BMI and WHO criteria,[14] i.e. normal: 18.5 kg/m^2 ≤ BMI ≤ 24.99 kg/m^2; overweight: 25 kg/m^2 ≤ BMI ≤ 29.99 kg/m^2; obesity: 30 kg/m^2 ≤ BMI ≤ 39.99 kg/m^2, morbid obesity: BMI ≥ 40 kg/m^2. Hypercholesterolaemia was defined as a total cholesterol level > 5.18 mmol/l.

The metabolic syndrome (MS) was defined according to the International Diabetes Federation (IDF) consensus criteria:[15] central obesity plus any two of the following: raised triglyceride levels ≥ 150 mg/dl (1.7 mmol/l) or specific treatment for this lipid abnormality, reduced HDL-C < 40 mg/dl (1.03 mmol/l) in men and < 50 mg/dl (1.29 mmol/l) in women or specific treatment for this lipid abnormality, raised blood pressure (≥ 130/85 mmHg) or treatment of previously diagnosed hypertension, raised fasting plasma glucose level ≥ 100 mg/dl (5.6 mmol/l) or previously diagnosed type 2 diabetes.[15]

Increased waist circumference was defined as > 102 cm for men and > 88 cm for women. With a BMI > 30 kg/m^2, central obesity was assumed without measurement of waist circumference.[15]

Alcohol consumption was categorised as low-to-moderate consumption (less than or equal to one local beer daily for women and two local beers for men) and excessive consumption (more than two local beers daily).[16] Smoking status was determined as current smokers, former smokers (having smoked in the past but having stopped for two or more weeks prior to the survey, however, those who had stopped within two weeks of the survey were considered current smokers), and never smoked.

Statistical analysis

Data analysis was done using the Statistical Package for Social Sciences (SSPS Inc, Chicago, IL) software version 20.0. Categorical variables were summarised as counts and percentages while continuous variables were summarised as means, median, standard deviation (SD) and percentiles where appropriate. Group comparisons used the chi-squared or Fisher's exact tests for categorical variables, and the Student *t*-test for continuous variables. A *p*-value < 0.05 was considered statistically significant.

Results

Table 1 shows the general characteristics of the study population. A total of 844 adults (57.4% were women and overall mean age was 52.6 ± 11.6 years) were included in the study, among whom 154 and 216, respectively, were from Cameroon and Nigeria, 240 from the DRC and 240 from Madagascar. The majority (76.6%) of the study participants were urban dwellers. The men were more likely to be employed and to be educated than the women (both $p < 0.001$). The women were more likely to be overweight, obese or morbidly obese than the men ($p < 0.001$). The men had a significantly higher mean triglyceride levels than the women (2.9 vs 2.2 mmol/l; $p = 0.019$) and lower mean HDL-C levels (1.6 vs 1.8 mmol/l; $p = 0.004$). Men also had higher mean normal values of serum creatinine (90.8 vs 75.7 µmol/l, $p < 0.001$) and uric acid (295.0 vs 233.2 µmol/l, $p < 0.001$) than the women. Men and women had similar mean systolic (149.5 vs 149.5 mmHg) and diastolic (91.9 vs 90.6 mmHg) blood pressures, respectively.

The overall prevalence of hypertension [previously aware/diagnosed (48.1%) and newly diagnosed (26%)] was 74.1% [Cameroon (91.5%), Nigeria (66.8%), DRC (99.1%) and Madagascar (45.0%)]. The overall prevalence of diabetes in the study was 15.7% and ranged from 24.8% in Nigeria, 15.6% in Cameroon and 15.0% in DRC, to 8.7% in Madagascar ($p = 0.003$). Excessive alcohol consumption was reported in 25.6% of study participants, with the highest prevalence in Cameroon (36.6%), and the lowest in Nigeria, where all participants reported low-to-moderate consumption ($p = 0.007$).

Of the study participants, 17.3% were either current or former smokers. A significant difference ($p < 0.001$) in prevalence of smoking across the countries was noted, with the highest prevalence in Madagascar (32.9%), followed by Cameroon (13%), then DRC (10.9%), and Nigeria (10.0%) being the lowest.

Of the study participants, 32.3 and 36.3% were overweight and obese (obesity 31.8%), or morbidly obese (4.5%), respectively. Overweight was highest in Madagascar (39.2%) and lowest in Nigeria (28.4%), while overall obesity was highest in Cameroon (53.6%) and lowest in Madagascar (10.0%) ($p < 0.001$). Details of the cardiometabolic risk factors across the countries are shown in Table 2.

When participants were assessed according to their hypertension status (Table 3), diabetes mellitus and hypercholesterolaemia

Table 1. General characteristics and overall profile of study population

	Cameroon (*n* = 154) 17.9%			Nigeria (*n* = 211) 25.9%			DRC (*n* = 239) 28.1%			Madagascar (*n* = 240) 28.1%			Total (*n* = 844)			
Variables	**Male (*n* = 54)**	**Female (*n* = 100)**	***p*-value**	**Male (*n* = 87)**	**Female (*n* = 124)**	***p*-value**	**Male (*n* = 116)**	**Female (*n* = 123)**	***p*-value**	**Male (*n* = 103)**	**Female (*n* = 103)**	***p*-value**	**Male (*n* = 360) (42.6%)**	**Female (*n* = 484) (57.4%)**	**Total (*n* = 844)**	***p*-value**
Age (years)	51.5 ± 9.7	56.4 ± 11.2	0.009	50.3 ± 13.2	48.8 ± 11.3	0.369	56.7 ± 11.2	55.7 ± 12.9	0.532	51.4 ± 10.0	49.5 ± 9.9	0.147	52.8 ± 11.5	52.3 ± 11.8	52.6 ± 11.7	0.512
BMI (kg/m²)	29.7 ± 3.8	31.1 ± 6.7	0.184	28.6 ± 6.1	31.2 ± 6.4	0.003	27.7 ± 6.8	30.4 ± 6.2	0.002	25.1 ± 4.0	25.0 ± 3.9	0.930	27.5 ± 5.8	29.3 ± 6.4	28.5 ± 6.1	0.000
BMI category, *n* (%)																
Normal	06 (11.1)	22 (22.0)		29 (33.4)	21 (16.8)		39 (33.6)	25 (20.4)		53 (51.4)	69 (50.4)		127 (35.3)	137 (28.3)	264 (31.3)	
Overweight	22 (40.7)	23 (23.0)	0.005	27 (31.0)	32 (25.8)	0.007	38 (32.8)	37 (30.1)	0.005	40 (38.8)	54 (39.4)	0.983	127 (35.3)	146 (30.2)	273 (32.3)	0.000
Obese	26 (48.2)	43 (43.0)		28 (32.2)	59 (47.7)		38 (32.8)	50 (40.6)		10 (9.7)	14 (10.2)		102 (28.3)	166 (34.3)	268 (31.8)	
Morbidly obese	00 (0.0)	12 (12.0)		03 (3.4)	12 (9.7)		01 (0.8)	11 (8.9)		00 (0.0)	00 (0.0)		04(1.1)	35 (7.2)	39 (4.6)	
WC (cm)	101.2 ± 12.8	102.7 ± 16.1	0.559	91.2 ± 11.5	97.4 ± 15.4	0.001	97.7 ± 17.9	99.9 ± 14.5	0.279	91.2 ± 11.2	88.4 ± 10.5	0.049	94.8 ± 14.5	96.6 ± 15.1	95.8 ± 14.8	0.071
HC (cm)	104.5 ± 12.3	109.4 ± 19.8	0.101	96.8 ± 12.6	106.2 ± 18.2	0.000	101.1 ± 10.0	110.6 ± 14.6	0.000	97.8 ± 7.5	99.4 ± 9.1	0.155	99.6 ± 10.8	106.1 ± 16.2	103.2 ± 14.5	0.000
SBP (mmHg)	168.5 ± 17.4	167.9 ± 17.8	0.855	138.8 ± 24.8	140.4 ± 25.7	0.656	163.6 ± 15.8	166.4 ± 21.2	0.260	132.3 ± 22.7	128.7 ± 23.1	0.231	149.5 ± 25.5	149.5 ± 27.9	149.3 ± 26.9	0.981
DBP (mmHg)	102.9 ± 11.4	100.4 ± 12.2	0.221	84.8 ± 11.8	86.2 ± 14.4	0.462	98.2 ± 11.5	96.4 ± 11.3	0.248	84.8 ± 13.9	82.2 ± 15.2	0.183	91.9 ± 14.4	90.6 ± 15.3	91.1 ± 14.9	0.239
History of HTN, *n* (%)																
Yes	01 (1.9)	05 (5.1)	0.423	50 (57.5)	82 (66.1)	0.248	81 (69.8)	93 (75.6)	0.383	38 (36.9)	55 (40.1)	0.688	170 (47.2)	235 (48.8)	405 (48.1)	0.729
No	53 (98.1)	93 (94.9)		37 (42.5)	42 (33.9)		35 (30.2)	30 (24.4)		65 (63.1)	82 (59.9)		190 (52.8)	247 (51.2)	437 (51.9)	
History of DM, *n* (%)																
Yes	06 (11.1)	09 (9.1)	0.778	10 (11.9)	12 (9.7)	0.820	11 (9.6)	14 (11.5)	0.677	06 (5.9)	02 (1.5)	0.077	33(9.3)	37(7.8)	70 (8.4)	0.452
No	48 (88.9)	90 (90.9)		74 (88.1)	104 (90.3)		104 (90.4)	108 (88.5)		97 (94.1)	135 (98.5)		323(90.7)	437(92.2)	760 (91.6)	
FBS (mmol/l)	6.2 ± 2.8	6.6 ±7.6	0.685	6.2 ±2.9	5.8 ± 4.1	0.979	5.4 ± 1.8	5.1 ± 1.6	0.084	5.9 ± 2.0	5.5 ± 1.6	0.122	5.8 ± 2.3	5.7 ± 4.2	5.8 ± 3.5	0.798
Lipid profile																
TG (mmol/l)	2.4 ± 10.0	0.9 ± 0.5	0.144	6.8 ± 5.8	5.8 ± 4.1	0.173	1.1 ± 0.6	1.0 ± 0.4	0.266	2.1 ± 1.4	1.4 ± 0.8	0.000	2.9 ± 5.3	2.2 ± 2.8	2.5 ± 4.1	0.019
HDL-C (mmol/l)	1.2 ± 0.5	1.3 ± 0.7	0.560	2.6 ± 1.1	2.9 ± 1.2	0.075	1.2 ± 0.3	1.4 ± 0.5	0.000	1.3 ± 0.6	1.5 ± 0.3	0.052	1.6 ± 0.9	1.8 ± 0.9	1.7 ± 0.9	0.004
LDL-C (mmol/l)	2.8 ± 0.8	2.5 ± 0.8	0.027	6.1 ± 3.3	6.5 ± 3.4	0.412	2.8 ± 1.2	2.9 ± 1.2	0.349	2.5 ± 0.8	2.7 ± 0.9	0.085	3.4 ± 2.3	3.6 ± 2.4	3.5 ± 2.4	0.436
TC (mmol/l)	4.4 ± 0.9	4.2 ± 0.9	0.317	8.8 ± 4.5	9.2 ± 4.8	0.549	4.5 ± 0.9	4.7 ± 1.1	0.154	4.8 ± 0.9	4.9 ± 1.1	0.360	5.5 ± 2.8	5.7 ± 3.0	5.6 ± 3.0	0.471
Creatinine (µmol/l)	108.6 ± 35.4	99.2 ± 40.4	0.153	56.2 ± 21.2	54.5 ± 28.4	0.658	107.2 ± 43.1	84.9 ± 22.1	0.000	88.8 ± 17.2	66.4 ± 11.4	0.000	90.8 ± 37.3	75.7 ± 31.1	82.1 ± 34.6	0.000
Uric acid (µmol/l)	384.6 ± 84.2	298.6 ± 119.9	0.000	300.7 ± 275.4	264.5 ± 242.1	0.350	405.3 ± 109.5	354.7 ± 100.1	0.000	340.6 ± 90.3	249.9 ± 67.9	0.000	295.0 ± 178.5	233.2 ± 154.1	259.3 ± 168.0	0.000
Alcohol intake, *n* (%)																
Low–moderate	22 (46.8)	49 (75.3)	0.003	–	–	–	52 (70.3)	45 (91.8)	0.006	38 (76.0)	20 (100.0)	0.014	114 (65.9)	115 (85.1)	229 (74.4)	0.000
Excessive	25 (53.2)	16 (24.7)					22 (29.7)	04 (8.2)		12 (34.0)	00 (0.0)		59 (34.1)	20 (14.9)	79 (25.6)	
Tobacco use, *n* (%)																
Current	05 (9.3)	05 (5.1)	0.004	04 (4.6)	00 (0.0)	0.000	10 (8.7)	01 (0.8)	0.000	26 (25.2)	22 (16.1)	0.007	45 (12.5)	28 (5.7)	73 (8.7)	0.000
Former	08 (14.8)	02 (2.0)		17 (19.7)	00 (0.0)		14 (12.2)	01 (0.8)		19 (18.4)	12 (8.7)		58 (16.1)	15 (3.1)	73 (8.7)	
Never	41 (75.9)	92 (92.9)		65 (75.7)	122 (100.0)		91 (79.1)	121 (98.4)		58 (56.3)	103 (75.2)		255 (71.4)	438 (91.2)	693 (82.6)	
Employment, *n* (%)																
Unemployed	0 (0.0)	14 (14.3)		01 (1.1)	06 (4.5)		12 (10.4)	16 (13.0)		02 (1.9)	06 (4.4)		15(4.1)	42(8.6)	57 (6.8)	
Full time	24 (44.4)	22 (22.4)		22 (24.4)	44 (35.3)		60 (51.7)	18 (14.6)		52 (50.5)	71 (51.8)		158(43.5)	155(31.8)	313 (37.2)	0.000
Part time	05 (9.3)	02 (2.0)	0.000	03 (3.3)	01 (0.8)	0.010	01 (0.8)	00 (0.0)	0.000	07 (6.8)	06 (4.4)	0.001	16(4.4)	09(1.9)	25 (2.9)	
Self-employed	13 (24.1)	09 (9.3)		46 (53.4)	50 (40.1)		24 (20.7)	18 (14.6)		29 (28.2)	24 (17.5)		112 (31.4)	101(21.4)	213 (25.3)	
Housewife	00 (0.0)	44 (44.9)		00 (0.0)	09 (7.2)		00 (0.0)	63 (51.2)		00 (0.0)	19 (13.8)		01 (0.3)	135(27.8)	136 (16.2)	
Retired	12 (22.2)	07 (7.1)		15 (17.8)	15 (12.1)		19 (16.4)	08 (6.5)		13 (12.6)	11 (8.0)		58 (16.3)	40(8.5)	98 (11.6)	
Education, *n* (%)																
None	01 (1.9)	15 (15.3)		01 (2.2)	11 (8.9)		02 (1.7)	18 (14.6)		00 (0.0)	01 (0.7)		04 (1.2)	45 (9.4)	49 (5.8)	
Primary school	12 (22.2)	38 (38.7)	0.000	54 (61.1)	70 (56.9)	0.113	05 (4.3)	31 (25.2)	0.000	11 (10.7)	12 (8.8)	0.024	82 (22.8)	151 (31.4)	233 (27.7)	0.000
High school	18 (33.3)	25 (25.5)		09 (10.0)	14 (11.4)		40 (34.5)	42 (34.1)		19 (18.4)	51 (37.2)		86 (23.8)	132 (27.4)	218 (25.9)	
Diploma	08 (14.8)	15 (15.3)		00 (0.0)	00 (0.0)		26 (22.4)	18 (14.6)		25 (24.3)	27 (19.7)		59 (16.4)	60 (12.5)	119 (14.1)	
Degree	15 (27.8)	05 (5.2)		23 (26.7)	28 (22.8)		43 (37.1)	14 (11.4)		48 (46.6)	46 (33.6)		129 (35.8)	93 (19.3)	222 (26.5)	
Residence, *n* (%)																
Urban	47 (87.0)	81 (82.6)	0.643	45 (51.7)	70 (56.9)	0.484	113 (97.4)	120 (97.5)	0.942	71 (68.9)	100 (72.9)	0.565	276 (76.6)	371 (77.1)	647 (76.9)	0.988
Semi-urban	07 (13.0)	17 (17.4)		42 (48.3)	53 (43.1)		03 (2.6)	03 (2.5)		32 (31.1)	37 (27.1)		84 (23.4)	110 (22.9)	194 (23.1)	

BMI = body mass index; WC = waist circumference; HC = hip circumference; SBP = systolic blood pressure; DBP = diastolic blood pressure; DM = diabetes mellitus; HTN = hypertension; FBS = fasting blood sugar; TG = triglycerides; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; TC = total cholesterol; DRC = Democratic Republic of Congo; *p*-values are for comparison between gender among participating countries.

were more common among participants with hypertension (17.7 vs 10.0%; $p = 0.010$ and 25.8 vs 18.0%; p = 0.008, respectively) than in normotensives. With regard to WC, 73.4% of women had a WC > 88 cm, most (79.4%) of whom were hypertensive, opposed to 67.7% who were non-hypertensive ($p = 0.004$). This difference was not statistically significant among the men. Overall, participants with hypertension were more likely to be overweight (33.2 vs 30.5%) and obese (42.5 vs 16.8%) ($p < 0.001$), but reported lower smoking rates (15.0 vs 24.1%; $p = 0.002$).

Hypertension and smoking were more prevalent in participants with diabetes (83.3 vs 71.9%; $p = 0.010$ and 19.7 vs 17.9%; $p =$ 0.019, respectively). The distribution of other risk factors, including hypercholesterolaemia, increased WC, overweight and obesity, and excessive alcohol consumption, was not significantly different between the participants with and without diabetes. Details of the risk factors according to presence or absence of diabetes are shown in Table 4.

The overall prevalence of the MS, impaired fasting glucose levels (IFG) and diabetes mellitus was 39.4, 9.3 and 15.7%, respectively. Detailed prevalences of the MS, IFG and diabetes according to urban or rural and hypertensive status, gender and country are presented in Fig. 1. The highest prevalence of the MS was reported

Table 2. Prevalence of selected risk factors across participating countries

Risk factor	Cameroon *n* (%)	Nigeria *n* (%)	DRC *n* (%)	Madagascar *n* (%)	Total *n* (%)	*p*-value
Hypertension (*n* = 844)						
Yes	141 (91.5)	141 (66.8)	237 (99.1)	108 (45.0)	630 (74.1)	0.000
No	13 (8.5)	70 (33.2)	02 (0.9)	132 (55.0)	220 (25.9)	
Diabetes (*n* n = 839)						
Yes	24 (15.6)	51 (24.8)	36 (15.0)	21 (8.7)	132 (15.7)	0.000
No	130 (84.4)	154 (75.2)	204 (85.0)	219 (91.3)	707 (84.3)	
Alcohol consumption (*n* = 309)						
Low–moderate	71 (63.4)	03 (100.0)	98 (79.0)	58 (82.8)	230 (74.4)	0.007
Excessive	41 (36.6)	00 (0.0)	26 (21.0)	12 (17.2)	79 (25.6)	
Smoking (*n* = 844)						
Current	10 (6.5)	04 (1.8)	11 (4.6)	48 (20.0)	73 (8.6)	0.000
Former	10 (6.5)	18 (8.5)	15 (6.3)	31 (12.9)	74 (8.7)	
Never	133 (87.0)	190 (89.7)	213 (89.1)	161 (67.1)	697 (82.7)	
Obesity (*n* = 844)						
Normal	28 (18.2)	53 (25.1)	64 (26.7)	122 (50.8)	267 (31.6)	
Overweight	45 (29.2)	60 (28.4)	76 (31.6)	94 (39.2)	275 (32.6)	0.000
Obese	69 (44.8)	85 (40.3)	88 (36.7)	24 (10.0)	266 (31.5)	
Morbidly obese	12 (8.8)	13 (6.2)	11 (5.0)	00 (0.0)	36 (4.3)	

p-values = comparison of variables across countries.

in Nigeria (62.1%), then Cameroon (45.2%), DRC (31.9%), and the lowest in Madagascar (27.7%).

IFG was most prevalent in Cameroon (15.3%), followed by Madagascar (10.4%), DRC (8.3%) and Nigeria (4.0%). Nigeria had the highest prevalence of diabetes (25.0%), then Cameroon (15.6%), DRC (15.0%) and finally Madagascar (8.7%). Both the MS and IFG were more prevalent in hypertensive patients than in non-hypertensive subjects (47.8 vs 8.3% and 10.1 vs 6.2%, respectively).

Table 3. Risk factors according to hypertension status in the study participants

Variable	Hypertensives *n* (%)	Non-hypertensives *n* (%)	Total (*n* = 844) *n* (%)	*p*-value
Tobacco smoking (*n* = 844)				
Current	42 (6.7)	31 (14.1)	73 (8.6)	0.002
Former	52 (8.3)	22 (10.0)	74 (8.8)	
Never	530 (85.0)	167 (75.9)	697 (82.6)	
Alcohol consumption (*n* = 309)				
Low to moderate	195 (73.6)	35 (79.5)	230 (74.4)	0.460
Excessive	70 (26.4)	09 (20.5)	79 (25.6)	
Obesity (*n* = 844)				
Normal	152 (24.3)	115 (52.7)	267 (31.5)	
Overweight	208 (33.2)	67 (30.5)	275 (32.5)	0.000
Obese	232 (37.1)	34 (15.9)	266 (31.5)	
Morbidly obese	34 (5.4)	02 (0.9)	36 (4.5)	
Waist circumference (*n* = 486)				
Men (> 102 cm)	76 (31.9)	86 (34.7)	162 (33.3)	0.564
Women (> 88 cm)	189 (79.4)	168 (67.7)	357 (73.4)	0.004
Diabetes mellitus (*n* = 839)				
Yes	110 (17.7)	22 (10.0)	132 (15.7)	0.007
No	509 (82.3)	198 (90.0)	707 (84.3)	
Hypercholesterolaemia (*n* = 811)				
Yes	102 (25.8)	75 (18.0)	177 (21.8)	0.008
No	293 (74.2)	341 (82.0)	634 (78.2)	

p-value = comparison of variables between the two groups.

Comparing gender, the MS was more prevalent in females (44.7 vs 32.1%), but incidence of IFG and diabetes was higher in males (13.6 and 17.2%) compared to females (6.2 and 12.7%), respectively. With regard to urban and rural status, the MS and diabetes were more prevalent in semi-urban dwellers (57 and 24.1%), opposed to urban dwellers (34.3 and 12.3%, respectively).

Discussion

In this self-selected group of participant in a hospital-based study of cardiometabolic risk factors among adults in four SSA countries, we found a high prevalence of the MS, IFG and diabetes mellitus in all countries. In spite of the differences observed between countries, which may reflect differences in healthcare access and resources, and possibly selection bias, these findings clearly signify the rapid growth of cardiovascular risk factors in a region of the world that has traditionally been known as the hotspot of nutritional and infectious diseases. This study is therefore relevant for understanding the epidemiology of cardiovascular and metabolic risk profiles of adults in the region, a pivotal step in the control of the incidence of CVDs.

The overall prevalence of the MS in our study population was 39.4% and ranged from 62.1% in Nigeria to 27.7% in Madagascar. This was particularly for hypertensive subjects, female participants and semi-urban dwellers. The overall prevalence of the MS was lower than reported in Ghana among hypertensive patients. It was however similarly observed that the MS was more prevalent among women than men (OR: 4.88, p = 0.027) in this study.[17] Another study among newly diagnosed type 2 diabetes subjects revealed higher prevalences of the MS of 68 and 81%, using IDF and WHO criteria, respectively. Again, as in our study, the MS was common in women and was driven essentially by female gender, family history of diabetes, overweight and obesity.[18]

IFG overall prevalence was 9.3% and ranged from 15.3% in Cameroon to 4.0% in Nigeria. Our findings are however higher than reported in a community-based study in South Africa,[19]

Table 4. Risk factors according to diabetes status in the study participants

Variable	Diabetes *n* (%)	Non-diabetes *n* (%)	Total *n* (%)	*p*-value
Tobacco smoking (*n* = 834)				
Current	07 (5.3)	66 (9.4)	73 (10.6)	
Former	19 (14.4)	54 (7.9)	73 (10.6)	0.019
Never	106 (80.3)	582 (82.7)	688 (78.8)	
Alcohol consumption (*n* = 308)				
Low to moderate	30 (69.7)	199 (75.0)	229 (75.1)	0.456
Excessive	13 (30.2)	66 (25.0)	79 (24.9)	
Obesity (*n* = 839)				
Normal	37 (28.0)	228 (32.2)	265 (31.6)	
Overweight	42 (31.8)	228 (32.2)	270 (32.2)	0.462
Obese	44 (33.3)	222 (31.6)	266 (31.7)	
Morbidly obese	09 (6.9)	29 (4.0)	38 (4.5)	
Waist circumference				
Men (> 102 cm) (*n* = 359)	10 (29.4)	85 (26.1)	95 (26.4)	0.685
Women (> 88 cm) (*n* = 478)	29 (76.3)	319 (72.5)	348 (72.8)	0.706
Hypertension (n = 839)				
Yes	110 (83.3)	509 (71.9)	619 (73.7)	0.007
No	22 (16.7)	198 (28.1)	220 (26.3)	
Hypercholesterolaemia (*n* = 809)				
Yes	15 (22.1)	161 (21.7)	176 (21.8)	0.949
No	53 (77.9)	580 (78.3)	633 (78.2)	

Diabetics = participants with diabetes mellitus; non-diabetics = participants without diabetes mellitus; *p*-values = comparison of variables between both groups.

and Nigeria.[20] These differences could be accounted for by the differences in study types (hospital based vs community based) and also geographical variations in the populations studied. However, the high prevalence of IFG among the participants is significant, as this represents a group of individuals at increased risk for transition to higher cardiovascular risk and the eventual development of diabetes if not properly controlled with lifestyle and dietary modifications.

Recent publications have highlighted the rapidly increasing prevalence of hypertension, coupled with under-diagnosis, undertreatment and low control rates in SSA.[4,20,21] The high prevalence of hypertension in our hospital-based study and the fact that 25.8% of these patients were newly diagnosed or undiagnosed cases is therefore not surprising. The situation was similar with diabetes mellitus, with an overall prevalence of 15.7%, with 6.9% being undiagnosed cases, as previously described.[22]

In a recent meta-analysis that focused on the burden of hypertension in Africa,[4] the pooled prevalence was 30%. Our prevalence is equivalent to the highest prevalence of 70% in the pooled studies. Another recent population-based study in Cameroon[21] reported a prevalence of 47.5%, which was lower than reported in our cohort.

The CLARIFY registry, which explored geographical variations in cardiovascular risk factors among coronary artery disease (CAD) patients, reported a high prevalence of hypertension of 48% in Eastern Europe.[23] The differences observed in these studies and others could be due to differences in populations studied and methodologies employed. Previous regional-based studies using similar methodology to ours are non-existent, therefore limiting the possibility for adequate comparison.

The high prevalence of diabetes in our study (15.7%) was slightly below the 17% noted among CAD patients in Eastern Europe but far lower than the 60% in the Middle East.[23] While we acknowledge the dearth of African regional data on diabetes, some national studies are worth noting. The highest prevalence of diabetes among participating countries was from Nigeria, with a prevalence rate of 24.8%. This was lower than the 28.2% noted in a community-based study in South Africa,[19] but higher than the 10.1% reported in a self-selected population study in Cameroon.[22] Variations in degree of urbanisation, and differences in lifestyle, environmental factors and study settings (population vs hospital based) as well as sample sizes most likely account for the differences seen in these studies.

Overall mean BMI of our study participants was 28.5 kg/m^2, which was higher than reported in Benin,[8] although it was lower than reported in Ghana among hypertensive subjects.[17] About one in three of the study participants was overweight or obese. This is likely to be explained by the increasing adoption of Western lifestyles, especially in urban areas (which were in the majority in our study), limited physical activity and increased sedentary lifestyles, which are wrongly attributed to good living. Similarly, a high prevalence of obesity has been reported in other parts of Africa,[8,17,24] in relation to urbanisation and high socio-economic status.[25] A community-based study in Cameroon by Fezeu and colleagues in 2010 demonstrated the influence of ethnicity and urbanisation on abdominal adiposity and obesityrelated abnormalities.[26]

A quarter of participants reported excessive alcohol consumption, and approximately one in five was either a current or former smoker. This is similar to the 19% smoking prevalence reported in Eastern Europe.[23] These are well-established drivers for CVD,[27] metabolic and other NCDs and most likely account in part for the high rates of hypertension, diabetes and obesity in our cohort. Our findings are supported by a recent meta-analysis of prospective studies on the association of alcohol consumption and CVD risk and mortality, where it was found that low-to-moderate alcohol consumption was inversely significantly associated with the risk of CVD and all-cause mortality among hypertensive patients.[27]

Risk profiles of the participants were examined according to hypertension status. A high prevalence of diabetes (17.7%) was noted among the hypertensive subjects, compared to 10% in non-hypertensives. This was half that reported in Ghana among hypertensive subjects,[17] although higher than the 13.5% reported in Cameroon.[28] Hypertensive patients were also more likely to be overweight and obese than non-hypertensive subjects, with prevalence rates of 33.1 and 42.8%, compared to 30.5 and 16.8%, respectively.

All other studied risk factors, such as hypercholesterolaemia, abdominal adiposity (WC > 88 cm for women and 102 cm for men), and excessive alcohol consumption were more prevalent among hypertensive subjects, except for smoking. The high prevalence of cardiometabolic risk factors reported in our study is similar to reports by Akintunde *et al*. among university staff in Nigeria.[20] Besides factors such as a high-salt diet, low physical activity and high socio-economic status (not examined in our study), these are established risk factors for hypertension, which in itself is a major risk for CVD. Urbanisation, among other determinants, has largely been queried.[8,19,29]

Our study showed that all risk factors studied were most prevalent among participants with diabetes. About three out of four diabetic subjects had hypertension. Other studies have reported a high prevalence of high blood pressure among diabetic subjects in

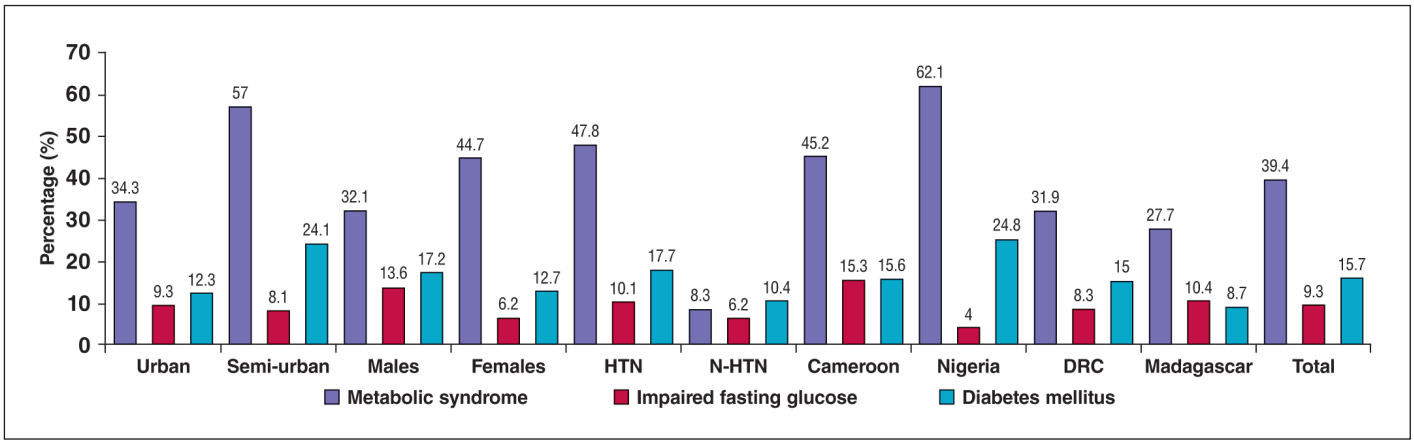

Figure 1. Prevalence of the metabolic syndrome, impaired fasting glucose levels and diabetes across countries, urbanicity, gender and hypertension status. HTN = hypertensives, N-HTN = non-hypertensives

Cameroon[30] and Tanzani,[31] although lower than in ours.

The higher prevalence of overweight, obesity (abdominal and general) as reflected in WC and mean BMI, hypercholesterolaemia, alcohol abuse and smoking, being more common in diabetic than non-diabetic subjects, is however an expected finding, as they all have individual and associative effects in predisposition to the development of diabetes.[8,30] Therefore, while diabetes in itself has been demonstrated to be an independent cardiovascular risk factor,[32] the impact of its association or cumulative effect with other traditional risk factors in the development, progression, morbidity and mortality linked with CVDs cannot be overemphasised.

Limitations and strengths of the study

Our study has several limitations that deserve mention. First the hospital base of the recruitments and the selected nature of the participants could have increased the chances that those included were at high risk for metabolic risk factors, which therefore could account for the high prevalence of cardiometabolic risk factors in our study. Secondly, the method of diagnosis of hypertension could be subject to debate, but it has been clearly evidenced by Burgess *et al*. that failure to carry out multiple measurements to confirm the diagnosis may lead to false positives.[33] Thirdly, quantity or concentration of alcohol in the local beer may vary from one country to another, and we could not assess non-industrial alcoholic beverages. Lastly, although the overall sample size was large, the number of patients contributed from each participating centre within the countries tended to be small, therefore precluding meaningful centre-level analysis.

In spite of these limitations, the multi-centre, multi-national character of this study increased our chances of adequately exploring the prevalence of cardiometabolic risk factors in the participating countries, and demonstrating evidence of the growing cardiovascular risk factors in this region plagued with communicable diseases. The use of well-trained data collectors (medical practitioners) also gave confidence in the measured parameters.

Conclusions

This study reports alarmingly high prevalences of cardiometabolic risk factors among adults presenting at urban and semi-urban hospitals in selected countries in SSA, which is in line with IDF projections of NCDs (hypertension and diabetes mellitus) in the region. It also raises the question of the influence of rapid urbanisation on the development of risk factors for imminent cardiovascular and metabolic diseases. This has considerable public health impact for an already economically disadvantaged setting to design new methods or further strengthen existing measures and interventions for the control of chronic diseases in the region.

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Telmisartan decreases microalbuminuria in patients with type 2 diabetes mellitus following coronary artery bypass grafting

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Abstract

Objective: **This prospective study aimed to investigate the effects of the selective angiotensin receptor antagonist, telmisartan, on microalbuminuria after coronary artery bypass surgery in patients with diabetes mellitus.**

Methods: **Patients were divided into two groups with block randomisation, using the sealed envelope technique: group T (telmisartan group) consisted of patients who received the angiotensin receptor blocking agent telmisartan 80 mg daily for at least six months in the pre-operative period; group N-T (non-telmisartan group) consisted of patients who received no telmisartan treatment. Clinical and demographic characteristics, operative and postoperative features, microalbuminuria and high-sensitivity C-reactive protein levels were compared.**

Results: **Forty patients met the eligibility criteria for the study. The groups did not differ with regard to clinical and demographic characteristics, and operative and postoperative features. Microalbuminuria levels between the groups differed significantly in the pre-operative period, first hour postoperatively and fifth day postoperatively. C-reactive protein levels between the groups differed significantly on the fifth day postoperatively.**

Conclusion: **Telmisartan was useful for decreasing systemic inflammation and levels of urinary albumin excretion in patients who had type 2 diabetes mellitus and had undergone coronary artery bypass surgery.**

Keywords: telmisartan, coronary artery bypass grafting, diabetes mellitus, microalbuminuria

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Microalbuminuria is considered to be a marker of endothelial dysfunction and is a predictor of cardiovascular disease and mortality.[1,2] Studies have implicated systemic vascular damage, extensive endothelial dysfunction, a glomerular haemodynamic state of hyperperfusion and hyperfiltration, a prothrombotic state, and a low-grade chronic inflammatory state.[3] Microalbuminuria is also associated with several cardiovascular disease risk factors, such as hyperglycaemia, hypertension, dyslipidaemia, renal dysfunction, obesity and smoking.[4] All of these factors contribute to the genesis of atherosclerosis.

Proteinuria is also an early marker for potentially serious renal disease in diabetics. It refers to an abnormally increased excretion rate of albumin in the urine, and is a sensitive indicator of generalised microvascular disease and a marker for vascular endothelial injury and multi-organ damage.[5] Reduction of microalbuminuria in diabetics may retard its progression to overt diabetic nephropathy.[5]

Once microalbuminuria is present, the rate of progression to end-stage renal disease can be delayed by inhibition of the renin–angiotensin system.[6] There is evidence that the use of agents that block the renin–angiotensin–aldosterone system, notably angiotensin receptor antagonists, may provide cardiovascular protection to diabetic patients with microalbuminuria.

Microalbuminuria increases following open-heart surgery where coronary artery bypass grafting (CABG) is utilised.[7] CABG activates an inflammatory cascade, which may increase capillary permeability and cause microalbuminuria. The increase in capillary permeability may induce exudation of proteins from the lung capillaries into the capillary–alveolar interspace and alveoli, causing the so-called postperfusion lung, which resembles pulmonary oedema. In a recent study, Loef *et al.* demonstrated that CABG potentiates transient renal failure and microalbuminuria.[8]

In this study, we aimed to investigate the effects of the selective angiotensin II receptor antagonist, telmisartan, on microalbuminuria after CABG surgery in patients with diabetes mellitus.

Methods

This observational study was approved by the local institutional review board (LUT/05/38/2006) and conducted in accordance with the amended Declaration of Helsinki and Good Clinical Practice

regulations. Written informed consent was obtained from all subjects. Patients admitted to the Department of Cardiovascular Surgery of our tertiary centre between June 2006 and February 2007 who had type 2 diabetes mellitus and had undergone CABG surgery constituted the study group.

Patients were divided into two groups with block randomisation, using the sealed envelope technique: group T (telmisartan group) consisted of patients who received the angiotensin receptor blocking agent, telmisartan (Micardis®, Boehringer Ingelheim, Istanbul, Turkey) 80 mg daily for at least six months in the pre-operative period; group N-T (non-telmisartan group) consisted of patients who received neither telmisartan nor any other angiotensin receptor blockers. In both groups, no patients were using angiotensin converting enzyme inhibitors for at least six months prior to the study.

Cases with severely impaired left ventricular function, chronic pulmonary obstructive disease, severe systemic non-cardiac disease, severe renal or liver impairment, infectious diseases before surgery, malignancy, those receiving corticosteroids or other immunosuppressive treatment, and patients with stroke, inflammatory disease, and/or previous cardiac surgery, and valvular heart disease were excluded from the study.

Surgical technique and postoperative care

Cardiac medication, including beta-adrenergic blocking agents, calcium channel blocking agents and nitrates, was continued until the morning of surgery. The same general anaesthetic drugs were used in all patients. A standard median sternotomy incision was used to expose the heart and place the internal mammary artery and saphenous vein grafts used for coronary anastomosis.

In each group, routine surgery was performed using a membrane oxygenator (Edwards Vital, Edwards Lifesciences LLC, Irvine, CA, USA), a 3-mg/kg dose of sodium heparin, 2 000 ml of Ringer's lactate primer and a roller pump at a body temperature of 28°C. Cardiopulmonary bypass was instituted via the ascending aorta and single two-stage venous cannulation (maintained at 2.2–2.4 l/min/m^2).

Following cross-clamping of the aorta, the heart was arrested using 10–15 cm^3/kg cold blood cardioplegia through the aortic root and topical ice slush was continued every 20 minutes for myocardial protection. Heparin was neutralised with protamine hydrochloride (Protamin 1000; Roche, Istanbul, Turkey). The circuit was primed with 2 000 ml Ringer's lactate.

After completion of the surgery, patients were transferred to the intensive care unit (ICU), where standard care and processes were followed until discharge. Patients were weaned from mechanical ventilation when they were haemodynamically stable, responding to verbal stimulation, and had been fully rewarmed. Patients were discharged from the ICU if they were haemodynamically stable, had normal blood gasses during spontaneous breathing, and had a satisfactory renal function.

Outcome parameters and other variables

Smoking, obesity, hypertension, duration of diabetes, family history of coronary artery disease, pre-operative myocardial infarction, and pre-operative haemodynamic data were recorded. During the surgical procedure, haemodynamic parameters, including heart rate, mean arterial pressure, central venous pressure, arterial blood gasses and urine output were monitored.

In the postoperative period in the ICU, cardiovascular and respiratory values and temperature were recorded every 15 minutes before extubation and then hourly until discharge from the ICU. The length of stay in the ICU was also recorded.

Microalbuminuria levels were studied pre-operatively, on the first hour postoperatively, and on postoperative days (POD) one and five. High-sensitivity C-reactive protein (hsCRP) levels were studied pre-operatively, and on POD 1 and 5. Patients who were considered to be in a low-cardiac output state received positive inotropic agents (dopamine or adrenaline or both). They were assessed for persistent systemic blood pressure below 90 mmHg, urinary output lower than 20 cm3/h, and the state of peripheral circulation was evaluated for adequate preload and optimal afterload. Urine samples were measured for microalbuminuria using Micral test sticks (Roche).

Statistical analysis

Categorical variables were analysed with chi-squared and Fisher's exact tests, as appropriate, in contingency tables, whereas the unpaired *t*-test and Mann–Whitney *U*-test were performed, as appropriate, for comparison of continuous variables. Comparisons for microalbuminuria and hsCRP levels in the groups were done with repeated measures of ANOVA and the Bonferroni test.

Data are expressed as means ± standard deviation. A p-value < 0.05 was considered statistically significant. All statistical analyses were performed with the Statistical Package for Social Sciences (SPSS 10.0 for Windows, SPSS, Inc., Chicago, IL).

The calculation of sample size was based on a power analysis. At a power of 80% using a significance level of $p < 0.05$, the sample size required was 20 subjects per study group.

Results

Forty patients met the eligibility criteria for the study. Of the 40 patients (29 males, 11 females) whose charts were reviewed, the average age was 65.0 ± 8.6 (range 40–79) years. Group T included 20 patients (15 males, 5 females) with a mean age of 65.6 ± 7.8 years, who had been using telmisartan 80 mg daily for at least six months. Group N-T included 20 patients (14 males, 6 females) with a mean age of 64.4 ± 9.5 years, who used no angiotensin receptor blocking agent prior to the operation. The groups were similar with regard to age and gender ($p = 0.680$ and $p = 0.723$, respectively).

With regard to clinical characteristics such as body mass index, smoking habit, hypertension, hyperlipidaemia, and history of myocardial infarct, the two groups did not show significant differences and were comparable (Table 1). The groups were also similar with regard to number of bypass grafts, cardiopulmonary bypass time, cross-clamp time, flow, atrial fibrillation, inotrope usage, time of endotracheal intubation and mortality rate (Table 2).

Table 1. Clinical and demographic characteristics of the study group

Characteristics	Group T	Group N-T	*p*-value
Age (years)	65.6 ± 7.8	64.4 ± 9.5	0.680
Gender (M/F)	15/5	14/6	0.723
Body mass index	28.0 ± 4.7	26.5 ± 2.8	0.234
Smoking, *n* (%)	11 (55)	10 (50)	0.752
Hypertension, *n* (%)	18 (90)	16 (80)	0.661
Hyperlipidaemia, *n* (%)	19 (95)	18 (90)	1.000
History of myocardial infract, *n* (%)	12 (60)	13 (65)	0.744

Group T = telmisartan group; group N-T = non-telmisartan group.

Table 2. Operative and postoperative features of the patients

Surgical parameters	Group T	Group N-T	*p*-value
Number of bypasses	2.9 ± 1.0	2.9 ± 0.9	0.876
Cardiopulmonary bypass time (min)	87.4 ± 31.3	86.6 ± 20.4	0.920
Cross-clamp time (min)	52.6 ± 21.6	53.2 ± 18.5	0.925
Flow (cm^3)	4469.0 ± 362.4	4491.0 ± 295.0	0.834
Atrial fibrillation, *n* (%)	4 (20)	6 (30)	0.716
Inotrope usage, *n* (%)	3 (15)	6 (30)	0.451
Mortality, *n* (%)	0	2 (10)	0.487

Group T = telmisartan group; group N-T = non-telmisartan group.

Pre-operative, first hour postoperative, POD 1 and POD 5 microalbuminuria levels were 16.5 ± 17.2, 28.5 ± 17.2, 59.0 ± 29.8 and 23.0 ± 20.0 mg/l in group T, and 30.0 ± 17.7, 51.0 ± 28.4, 75.0 ± 25.6 and 52.5 ± 27.5 mg/l in Group N-T, respectively, and there were statistically significant differences between four microalbuminiria levels in each group ($p < 0.001$) (Table 3). Pre-operative, first hour postoperative and POD 5 values were statistically significantly different between the groups ($p = 0.018$, $p = 0.008$ and $p = 0.001$, respectively) (Table 3). However, the difference in POD 1 values between the groups was at the threshold of significance ($p = 0.071$).

Pre-operative plasma levels of hsCRP (0.35 ± 0.17 vs 0.50 ± 0.32 mg/l) showed a trend towards significance ($p = 0.069$). Although POD 1 hsCRP levels (10.0 ± 2.0 vs 17.8 ± 3.9 mg/l) did not differ ($p = 0.405$) between the groups, a decrease in POD 5 hsCRP levels in group T (8.6 ± 2.9 vs 10.9 ± 3.2 mg/l) was statistically significant between the groups ($p = 0.024$) (Table 4).

All CABG surgeries were performed successfully. There was no repeat surgery for bleeding or peri-operative myocardial infarction in either group. The only complication was one cerebrovascular accident in the N-T group. There was no clinical or laboratory evidence of postoperative renal dysfunction in either group. Urine output during surgery and in the postoperative period did not differ between the groups. No wound infection was observed for any patient.

Discussion

Coronary artery bypass grafting is often followed by a systemic inflammatory response. The clinical relevance of CABG- related systemic inflammation varies with patients and such inflammation may be accompanied by intermittent organ dysfunction and finally, multi-organ failure, including renal and pulmonary dysfunction.[9,10]

In some patient groups, the effect of extracorporeal circulation is serious after open-heart surgery and it is well known that diabetic patients are frequently associated with renal and cardiovascular disease, requiring surgical and medical intensive care. Some pathophysiological mechanisms such as microalbumiuria and urinary protein over-excretion are responsible for these damaging effects in this particular group of patients.

Table 3. Pre- and postoperative microalbuminuria levels

	Group T Mean ± SD	Group N-T Mean ± SD	*p*-value
Pre-operative	16.5 ± 17.2	30.0 ± 17.7	0.018
Postoperative 1st hour	28.5 ± 17.2	51.0 ± 28.4	0.008
Postoperative 1st day	59.0 ± 29.8	75.0 ± 25.6	0.071
Postoperative 5th day	23.0 ± 20.0	52.5 ± 27.5	0.001

Group T = telmisartan group; group N-T = non-telmisartan group; SD = standard deviation.
Group T: Pre-op vs 1st day: $p < 0.001$; pre-op vs 5th day: $p = 0.036$; 1st hour vs 5th day: $p = 0.021$; 1st day vs 5th day: $p = 0.036$.
Group N-T: Pre-op vs 1st day: $p < 0.001$; 1st hour vs 1st day: $p < 0.001$; 1st hour vs 5th day: $p < 0.001$; 1st day vs 5th day: $p < 0.001$.

Table 4. High-sensitivity C-reactive protein levels (mg/l)

	Group T Mean ± SD	Group N-T Mean ± SD	*p*-value
Pre-operative	0.35 ± 0.17	0.50 ± 0.32	0.069
Postoperative 1st day	10.0 ± 2.0	17.8 ± 3.9	0.405
Postoperative 5th day	8.6 ± 2.9	10.9 ± 3.2	0.024

Group T = telmisartan group; group N-T = non-telmisartan group; SD = standard deviation.

In patients with diabetes, angiotensin II is believed to play a main role in the progression of renal damage, not only through haemodynamic effects but also non-haemodynamic effects, including stimulation of growth factors and cytokines and changes in extracellular matrix metabolism.[11] Angiotensin II gives rise to glomerular hypertension and can alter the filtration properties of the glomerular basement membrane, leading to proteinuria.[12-13] Angiotensin receptor antagonists have been shown to consistently produce favourable mortality and morbidity outcomes in endpoint trials in patients with type 2 diabetes and diabetic nephropathy.[14-16]

Microalbuminuria refers to the increased excretion of albumin into the urine, which is so slight that it can be detected only by sensitive immunological analysis. Microalbuminuria is measured in diabetic patients to predict incipient nephropathy. The predictive value of microalbuminuria for the expression of cardiovascular diseases has also been investigated and, in fact, is as powerful for predicting hyperlipidaemia or hypertension.[17]

Microalbuminuria also occurs in acute conditions where capillary permeability increases. Microalbuminuria increases during major surgery such as CABG, and extracorporeal circulation activates an inflammatory cascade, which may increase capillary permeability and cause microalbuminuria. The increase in capillary permeability may induce exudation of proteins from the lung capillaries into the capillary–alveolar interspace and alveoli, causing the so-called post-perfusion lung, which resembles pulmonary oedema.

We found that telmisartan, as an angiotensin II receptor antagonist, had a significant lessening effect on microalbuminuria in type 2 diabetes patients undergoing coronary bypass surgery in our study. A significant decrease in hsCRP levels on day 5 was also noticed between the groups.

Several previous studies have shown that angiotensin receptor antagonists are effective anti-inflammatory agents, and our patients receiving telmisartan revealed decreased levels of systemic inflammation after CABG. This anti-inflammatory effect of telmisartan may help preserve postoperative renal function and also vascular endothelial function, which may also be seen after bypass surgery.

We know that renal dysfunction is a serious complication of coronary revascularisation with CABG and results in increased morbidity and mortality rates and prolonged hospital stay.[18] The injurious action of CABG on renal function is caused by several mechanisms, including non-pulsatile perfusion and increased levels of circulating catecholamines, cytokines and free haemoglobin.[19] These effects result in damage to the glomerular as well as tubular structures, which, in turn, may cause renal dysfunction, especially in the presence of additional risk factors.[20-21]

Microalbuminuria is one of the sensitive markers of increased capillary permeability and may be useful to study the systemic inflammatory response after CABG.[6,22,23] According to previous investigations, urinary microalbuminuria increased significantly in the early postoperative period and one day after CABG.

In our study, peak increase in microalbuminuria was observed in both groups but there was no statistically significant difference ($p = 0.071$). These levels decreased, particularly on the fifth day in our cases, and the decrease was statistically significantly different in group T. In both groups, hsCRP increased and peaked on the first postoperative day in both groups. However, in group T, hsCRP, as one of the pro-inflammatory agents, decreased significantly on the fifth day. Therefore, the increase in acute inflammatory response was similar in both groups on the first postoperative day, and in group T, both markers had decreased by the fifth day.

Borch-Johnsen *et al.* showed the direct relationship between proteinuria and cardiovascular mortality rate in insulin-dependent diabetic patients after open-heart surgery in patients undergoing CABG.[24] Telmisartan was also shown to reduce or normalise microalbuminuria in 34% of patients with diabetes, and in a second, smaller study including 64 hypertensive and 60 normotensive patients, to reduce the incidence of renal dysfunction. This confirmed that telmisartan reduced microalbuminuria independently of its blood pressure-lowering effects. Restoration of normal urine albumin levels has also been demonstrated by telmisartan.[25]

Our study showed that telmisartan reduced microalbuminuria, not only pre-operatively, but also after open-heart surgery. The return to baseline levels was also faster than in group N-T. Angiotensin receptor blocking agents decrease some of the postoperative acute inflammatory agents in on-pump CABG patients with diabetes mellitus by lessening the systemic consequences of renal dysfunction, and may have additional cardiovascular effects by exerting beneficial effects on endothelial tissue elsewhere in the body and within the heart in this patients group. The cardiovascular benefits of angiotensin receptor antagonists have been evaluated, not only in terms of their ability to lower blood pressure, but also on their ability to prevent strokes, cardiac events and target-organ damage.[14,16]

Limitations of our study are the relatively small size of our series and the lack of definite criteria for selection of patients for this study. As most coronary patients are already being treated with angiotensin receptor blocking agents, the results of our study will not have a major impact on clinical practice. Furthermore, it would have been better to test the predictive value of microalbuminuria on prognosis in this category of patients. However, we hope that this study will pioneer further studies on this method.

Conclusion

Our results showed that telmisartan decreased systemic inflammation and urinary albumin excretion in diabetic patients after CABG surgery, compared to those not taking angiotensin receptor antagonists. These beneficial effects of telmisartan treatment on diabetic patients after CABG should be investigated further in prospective, randomised studies.

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Red cell distribution width is correlated with extensive coronary artery disease in patients with diabetes mellitus

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Abstract

Introduction: **Previous studies have predicted an independent relationship between red cell distribution width (RDW) and the risk of death and cardiovascular events in patients with coronary artery disease (CAD). The aim of this study was to investigate the relationship between RDW and extensiveness of CAD in patients with diabetes mellitus (DM).**

Methods: **Two hundred and thirty-three diabetic patients who underwent coronary angiographies at our centre in 2010 were included in the study. All of the angiograms were re-evaluated and Gensini scores were calculated. Triple-vessel disease was diagnosed in the presence of stenosis > 50% in all three coronary artery systems.**

Result: **RDW was significantly higher in diabetic CAD patients ($p < 0.001$). Patients with CAD who had a RDW value above the cut-off point also had higher Gensini scores, higher percentages of obstructive CAD and triple-vessel disease ($p \leq 0.001$ for all). According to the cut-off values calculated using ROC analysis, RDW > 13.25% had a high diagnostic accuracy for predicting CAD. RDW was also positively correlated with Gensini score, obstructive CAD and triple-vessel disease ($r < 0.468$ and $p < 0.001$ for all).**

Conclusion: **RDW values were found to be increased in the diabetic CAD population. Higher RDW values were related to more extensive and complex coronary lesions in patients with DM.**

Keywords: red cell distribution width, coronary artery disease, diabetes mellitus, Gensini score

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Red cell distribution width (RDW) is widely accepted as a measure of anisocytosis and is routinely reported during automated complete blood counts.[1] It is commonly used to narrow the differential diagnosis of anaemia.[2] Many studies have reported that higher RDW values are associated with a worse prognosis in coronary artery disease, heart failure, peripheral artery disease, and even in the unselected population.[3-6]

Diabetes mellitus (DM) is one of the major risk factors for atherosclerosis.[7] Coronary artery disease (CAD) is more common among patients with DM.[8] CAD is the main cause of death in DM, and DM is associated with a two- to four-fold increased mortality risk from heart disease.[9] Moreover, it has a worse prognosis and is usually more advanced at the time of diagnosis.[10]

Previous studies have shown an association between RDW value and the severity of CAD, but there were no data on the diabetic population.[11-13] The aim of this study was to investigate the relationship between RDW and the extensiveness of CAD in patients with DM.

Methods

The study group was formed retrospectively from our catheterisation laboratory registries. Two hundred and thirty-three diabetic patients who underwent coronary angiography at our centre in 2010 were included in the study. The diagnosis of DM was based on a previous history of diabetes treated with or without drug therapies.

Patients with acute or chronic inflammatory disease, severe liver or renal insufficiency, morbid obesity, malignancy, valvular heart disease, heart failure, prior coronary intervention, or who had experienced acute coronary syndrome within 30 days prior to coronary angiography were excluded from the study. In addition, subjects were also excluded if they had a history of anaemia and blood transfusion.

Patient age, gender, past history of disease, smoking habits and current medications were carefully ascertained. Hypertension was defined as blood pressure ≥ 140/90 mmHg or if the subject was taking antihypertensive medications. Dyslipidaemia was defined as low-density lipoprotein cholesterol ≥ 100 mg/dl (≥ 2.59 mmol/l) or if they were taking a hypolipidaemic drug. Anaemia was defined as haemoglobin concentration < 13 mg/dl in men and < 12 mg/dl in women. Body mass index (BMI) was calculated as weight/height^2 (kg/m^2).

This investigation was a single-centre study. Informed consent was obtained from all participants, and the study protocol was approved by the ethics committee at our institution. The study was in accordance with the Declaration of Helsinki.

Blood samples were drawn from each patient after overnight fasting, during admission for routine chemistry. Haemoglobin, white blood cell count, mean platelet volume (MPV) and RDW values were measured with a Pentra DX 120 analyser (ABX, Montpellier, France).

Neutrophil/lymphocyte (N/L) ratio was calculated by dividing the total neutrophil count by the lymphocyte count.

High-sensitivity C-reactive protein (hs-CRP) analyses were done using the immunonephelometry method (Dade Behring, Inc, BN Prospect, Marburg, Germany). Serum levels of creatinine, fasting blood glucose, triglycerides, total cholesterol, and low- and high-density lipoprotein cholesterol were measured using conventional methods.

A conventional angiography device (Artis zee; Siemens, Erlangen, Germany) was used for coronary angiography. Angiograms were evaluated qualitatively by two different experts, and mean values were used to assess the rate of stenosis. Patients with atherosclerotic lesions in any of the coronary arteries were diagnosed as having CAD. Obstructive CAD was defined as stenosis of ≥ 50% of the diameter of a major epicardial or branch vessel > 2.0 mm in diameter.

Gensini scores were calculated for each patient as previously defined.[14] Triple-vessel disease was defined as stenosis of ≥ 50% in each of the major vessels or their major branches. Patients were evaluated and treated according to the current guidelines.

Table 1. Baseline characteristics and laboratory findings of the study groups

Variables	CAD– (*n* = 109)	CAD+ (*n* = 124)	*p*-value
Age (years)	58.6 ± 8.0	57.7 ± 9.0	0.387
Gender (male)	61 (56)	68 (55)	0.895
Hypertension	93 (85)	104 (84)	0.856
Dyslipidaemia	61 (56)	77 (62)	0.353
Smoking	14 (13)	24 (20)	0.215
Aspirin	72 (66)	93 (75)	0.150
Clopidogrel	0 (0)	23 (19)	< 0.001
RAS blockers	70 (64)	93 (75)	0.086
β-blockers	34 (31)	66 (53)	0.001
Calcium channel blockers	20 (18)	23 (19)	1.000
Statins	30 (28)	43 (38)	0.260
Body mass index (kg/m²)	28.7 ± 5.0	28.3 ± 4.5	0.536
Systolic blood pressure (mmHg)	130 ± 13	132 ± 14	0.144
Diastolic blood pressure (mmHg)	78 ± 9	79 ± 8	0.627
Glucose (mg/dl)	166 ± 75	174 ± 78	0.416
[mmol/l]	[9.21 ± 4.16]	[9.66 ± 4.33]	
Creatinine (mg/dl)	0.73 ± 0.18	0.71 ± 0.28	0.630
[µmol/l]	[64.53 ± 15.91]	[62.76 ± 24.75]	
Uric acid (mg/dl)	4.5 ±1.4	4.9 ± 1.7	0.081
hs-CRP (mg/l)	5.12 ± 2.93	6.07 ± 4.83	0.348
Total cholesterol (mg/dl)	197 ± 40	199 ± 49	0.726
[mmol/l]	[5.10 ± 1.04]	[5.15 ± 1.27]	
Triglycerides (mg/dl)	187 ± 86	191 ± 138	0.786
[mmol/l]	[2.11 ± 0.97]	[2.16 ± 1.56]	
LDL cholesterol (mg/dl)	120 ± 36	122 ± 44	0.688
[mmol/l]	[3.11 ± 0.93]	[3.16 ± 1.14]	
HDL cholesterol (mg/dl)	46 ± 11	45 ± 13	0.283
[mmol/l]	[1.19 ± 0.28]	[1.17 ± 0.34]	
WBC (103 cells/µl)	7.0 ± 1.9	7.2 ± 2.0	0.407
Haemoglobin (g/dl)	13.1 ± 1.1	13.1 ± 1.6	0.757
RDW (%)	12.5 ± 1.5	13.8 ± 1.7	< 0.001
MPV (fl)	8.43 ± 1.10	8.59 ± 1.02	0.265
Neutrophil/lymphocyte ratio (%)	2.26 ± 1.37	2.52 ± 1.94	0.457

CAD: coronary artery disease, CAD–: patients with normal coronary arteries, CAD+: patients with coronary artery disease, RAS: renin–angiotensin system, hs-CRP: high-sensitivity C-reactive protein, LDL: low-density lipoprotein, HDL: high-density lipoprotein, WBC: white blood cells, RDW: red cell distribution width, MPV: mean platelet volume. Data are shown as n (%) or mean ± SD

Table 2. Baseline characteristics and laboratory findings of low and high RDW groups

Variables	Low RDW (≤ 13.25) (*n* = 46)	High RDW (> 13.25) (*n* = 78)	*p*-value
Age (years)	56.7 ± 8.0	58.2 ± 9.5	0.381
Gender (male)	27 (59)	41 (53)	0.318
Hypertension	38 (83)	66 (85)	0.478
Dyslipidaemia	29 (63)	48 (61)	0.511
Smoking	5 (11)	19 (24)	0.052
Aspirin	33 (72)	60 (77)	0.331
Clopidogrel	11 (24)	12 (15)	0.173
RAS blockers	32 (70)	61 (78)	0.195
β-blockers	28 (61)	38 (49)	0.130
Calcium channel blockers	9 (20)	14 (18)	0.501
Statins	13 (28)	30 (39)	0.169
Body mass index (kg/m²)	28.8 ± 4.5	28.0 ± 4.5	0.363
Systolic blood pressure (mmHg)	131 ± 13	133 ± 15	0.328
Diastolic blood pressure (mmHg)	78 ± 8	79 ± 8	0.196
Glucose (mg/dl)	163 ± 77	181 ± 79	0.207
[mmol/l]	[9.05 ± 4.27]	[10.05 ± 4.38]	
Creatinine (mg/dl)	0.63 ± 0.17	0.76 ± 0.31	0.008
[µmol/l]	[55.69 ± 15.03]	[67.18 ± 27.40]	
Uric acid (mg/dl)	4.6 ± 1.5	5.1 ± 1.7	0.213
hs-CRP (mg/l)	4.11 ± 1.88	7.12 ± 5.58	0.043
Total cholesterol (mg/dl)	195 ± 44	202 ± 52	0.481
[mmol/l]	[5.05 ± 1.14]	[5.23 ± 1.09]	
Triglycerides (mg/dl)	197 ± 173	188 ± 114	0.736
[mmol/l]	[2.23 ± 1.95]	[2.12 ± 1.29]	
LDL cholesterol (mg/dl)	114 ± 33	127 ± 48	0.088
[mmol/l]	[2.95 ± 0.85]	[3.29 ± 1.24]	
HDL cholesterol (mg/dl)	46 ± 15	44 ± 12	0.461
[mmol/l]	[1.19 ± 0.39]	[1.14 ± 0.31]	
WBC (103 cells/µl)	7.1 ± 1.9	7.3 ± 2.2	0.516
Haemoglobin (g/dl)	13.3 ± 1.5	13.0 ± 1.6	0.454
RDW (%)	12.9 ± 0.7	14.3 ± 1.4	0.001
MPV (fl)	8.35 ± 1.13	8.72 ± 0.93	0.049
Neutrophil/lymphocyte ratio (%)	1.92 ± 0.07	2.89 ± 2.33	0.009

RDW: red cell distribution width, RAS: renin–angiotensin system, hs-CRP: high-sensitivity C-reactive protein, LDL: low-density lipoprotein, HDL: high-density lipoprotein, WBC: white blood cells, MPV: mean platelet volume.
Data are shown as n (%) or mean ± SD

Statistical analysis

Statistical analysis was performed using commercial software (IBM SPSS Statistics 22, SPSS Inc, Chicago, IL, USA). After performing the Kolmogorov–Smirnov normality test, two independent-sample *t*-tests were used to compare the normally distributed independent variables, and the Mann–Whitney *U*-test was used to compare the non-normally distributed independent variables between the two groups. For normally distributed variables, mean and standard deviation (SD) are listed, otherwise, median values are given. To analyse the categorical data, a chi-squared test was used. Categorical data are expressed as numbers and percentages.

A receiver operating characteristic (ROC) curve was constructed for RDW to test the effectiveness of various cut-off points in predicting CAD. The area under the ROC curve was calculated; the sensitivity and specificity for the RDW of the most appropriate cut-off point were calculated for predicting CAD. Correlations were determined using the Spearman test. A p-value < 0.05 was considered statistically significant.

Results

The study group was divided into two, according to angiographic results (CAD negative and CAD positive). There were no significant differences between the two groups with regard to age, gender, hypertension, hyperlipidaemia, smoking, BMI, systolic and diastolic blood pressure, and medications, including aspirin, renin–angiotensin system (RAS) blockers and statins (Table 1).

Clopidogrel and calcium channel blocker use was higher in the CAD-positive group ($p < 0.001$ and $p = 0.001$, respectively) (Table 1). There were no differences between the two groups in serum levels of glucose, creatinine, uric acid, hs-CRP, lipid profile, WBC, haemoglobin, MPV and N/L ratio (Table 1). RDW was significantly higher in the CAD-positive group (12.5 ± 1.5 vs 13.8 ± 1.7%, $p < 0.001$) (Table 1).

The most appropriate cut-off point calculated for predicting CAD was 13.25%. The patients who had a RDW ≤ 13.25% were included in the low RDW group. The rest formed the high RDW group.

There were no significant differences between the low and high RDW groups with regard to age, gender, hypertension, hyperlipidaemia, smoking, BMI, systolic and diastolic blood pressure and medications (Table 2). There were also no differences between the low and high RDW groups with regard to serum levels of glucose, uric acid, lipid profile, WBC and haemoglobin (Table 2).

Serum levels of creatinine, hs-CRP, MPV and N/L ratio were significantly higher in the high RDW group ($p < 0.005$ for all) (Table 2). RDW was positively correlated with hs-CRP, MPV and N/L ratio ($r = 0.248$, $r = 0.240$ and $r = 0.281$, respectively and $p = 0.033$ for hs-CRP, $p < 0.001$ for MPV and N/L ratio).

Patients with CAD who had a RDW value above the cut-off point also had higher Gensini scores, higher percentages of obstructive CAD and triple-vessel disease ($p \leq 0.001$ for all) (Table 3). According to the cut-off values calculated using ROC curve analysis, RDW > 13.25% had a high diagnostic accuracy for predicting CAD (area under the ROC curve = 0.742, $p < 0.001$) (Table 4, Fig. 1). RDW was positively correlated with Gensini score, obstructive CAD and triple-vessel disease ($r = 0.468$, $r = 0.409$ and $r = 0.332$, respectively and $p < 0.001$ for all).

Table 2. Baseline characteristics and laboratory findings of low and high RDW groups

Variables	Low RDW (≤ 13.25) (*n* = 46)	High RDW (> 13.25) (*n* = 78)	*p*-value
Gensini score			
Total	11 [4–31]	43 [16–73]	< 0.001
LAD	5 [3–12]	18 [5-30]	0.001
Cx	3 [1–5]	7 [3–19]	< 0.001
RCA	2 [1–3]	7 [2–18]	< 0.001
Obstructive CAD	23 (50)	63 (81)	0.001
Triple-vessel disease	2 (4)	26 (33)	< 0.001

RDW: red cell distribution width, LAD: left anterior descending coronary artery, Cx: circumflex coronary artery, RCA: right coronary artery, CAD: coronary artery disease. Data are shown as n (%) or median [interquartile range].

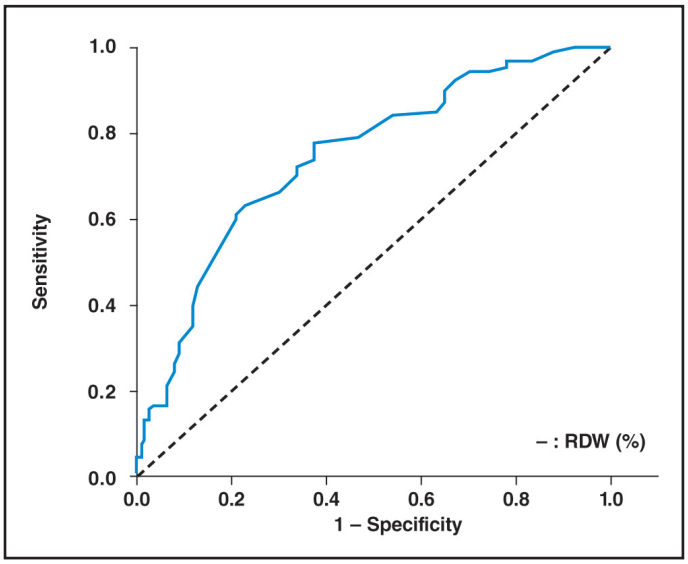

Figure 1. Receiver operating characteristic curve showing the relationship between sensitivity and false positivity at various cut-off points for red cell distribution width to predict coronary artery disease.

Discussion

This study showed an association between RDW and CAD in diabetic patients. RDW values were found to be higher in the diabetic CAD population and higher RDW values were related to more extensive and complex coronary lesions.

RDW is a marker of the variation in size of red blood cells circulating in the body, which reflects the value of anisocytosis.[1] It is routinely reported during automated complete blood counts. An elevation in RDW values may be seen in patients with ineffective erythropoiesis (iron, vitamin B_{12} or folic acid deficiency and various haemoglobinopathies), recent blood transfusions and haemolysis.[15] In daily practice it is commonly used to narrow the differential diagnosis of anaemia.[2]

The growing attention given to the relationship between RDW and cardiovascular events was first spurred on by the report from Felker *et al*., which concluded that there was a strong and independent association between RDW and the risk of adverse outcomes in heart failure patients.[16] Subsequently, Tonelli *et al*. predicted an independent relationship between RDW and the risk of cardiovascular death in patients with CAD.[3,16] Following the direction of these studies, researchers reported that higher RDW values were also associated with a worse prognosis in peripheral artery disease and even in the unselected population.[5,6]

Several explanations could be postulated in order to explain the underlying mechanisms that may contribute to a worse prognosis among patients with cardiovascular disease. However the reason for the poor prognosis remains unclear.

It has not been determined yet whether RDW is a marker of the severity of various disorders or if there is direct link between

Table 4. Diagnostic accuracy of red cell distribution width for coronary artery disease

Variable	Cut-off value	AUC	95% CI of AUC	Sensitivity	Specificity	*p*-value[a]
RDW (%)	> 13.25	0.742	0.679–0.806	0.629	0.771	< 0.001

AUC: area under the receiver operating characteristic curve, CI: confidence interval, RDW: red cell distribution width. aSignificance level of AUC.

anisocytosis and poor prognosis in patients with CAD. Factors impairing bone marrow haematopoiesis are probably identical to those that worsen the prognosis in CAD. These factors are anaemia, iron deficiency, lipid disorders, chronic inflammation, neurohumoral activation, glycaemic disturbance, vitamin D_3 deficiency, oxidative stress and renal failure.[17,18] Additionally, red cell deformability diminution may result in impaired flow through the microcirculation.[17]

Previous studies have shown an association between RDW and the severity of CAD.[11-13] Akin *et al*. investigated the association of RDW with the severity of CAD in acute myocardial infarction and showed that higher RDW values were correlated with higher Syntax scores, which means more complex coronary lesions. They found that after multiple logistic regression analysis, RDW remained a significant predictor for the severity of CAD.[11] Isik *et al*. evaluated this relationship in patients with stable angina pectoris and found an independent association between RDW and the complexity of CAD, which was determined with Syntax scores.[12]

A large Chinese cohort study with 677 subjects showed significantly elevated RDW values in CAD patients and a positive correlation between RDW and the Gensini score.[13] They also found that a RDW value of 12.85% was an effective cut-off point for predicting CAD, with a sensitivity of 50% and a specificity of 65%. Recently, Sahin *et al*. concluded that RDW values were independently associated with a high Syntax score but were not associated with long-term mortality in patients with non-ST-elevation myocardial infarction.[19]

In agreement with the current literature, we found that elevation in RDW values was associated with both the presence and complexity of CAD. Furthermore, we found that an RDW value of 13.25% was an effective cut-off point in order to determine the presence of CAD. Moreover, our study is the first to show an association between RDW and CAD severity in a diabetic population.

Chronic inflammation and neurohumoral activation are thought to be the key factors for both a worse cardiovascular prognosis and more complex coronary lesions.[17,18] In our study, hs-CRP levels were similar in the two CAD groups, but there was a positive correlation between RDW and hs-CRP. Unfortunately, we did not measure brain natriuretic peptides, which are markers of the neurohumoral pathway. Some researchers demonstrated that elevated mean platelet volume (MPV) was associated with acute coronary syndromes, thrombosis and inflammation.[20,21] We also found a positive relationship between RDW and MPV.

It is well known that there is a link between glycaemic disturbance and high RDW values. Two different studies showed a relationship between glycosylated haemoglobin and RDW in an unselected elderly population and in healthy adults.[22,23] Garg *et al*. demonstrated that glycosylated haemoglobin was an independent predictor of CAD severity in a non-diabetic population.[24] Our findings support the results of previous studies.

This study has some limitations. First, we did not measure some factors that might have influenced RDW levels, such as vitamin B_{12}, folate and iron levels. Second, cardiovascular events were not analysed due to the cross-sectional nature of the study. Third, the relationship between RDW, glycaemic disturbance and the severity of CAD could have been better understood if we had analysed glycosylated haemoglobin levels. Lastly, the diagnosis of DM was based on a previous history instead of biochemical results.

Conclusion

RDW values were significantly higher in diabetic than non-diabetic patients with CAD. Higher RDW values were related to more extensive and complex coronary lesions, suggesting that RDW may be a marker for predicting CAD severity in patients with DM.

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Anabolic androgenic steroids may be associated with early coronary artery disease

Anabolic androgenic steroids may be associated with early coronary artery disease, according to research presented at the Brazilian Congress of Cardiology 2017. 'Anabolic androgenic steroid abuse among young people is a widespread problem worldwide, and adverse events such as sudden cardiac death and heart attack have been reported in athletes,' said lead author Francis Ribeiro de Souza, PhD student, Heart Institute, Medical School, University of São Paulo, Brazil.

'In Brazil, around one million people have used anabolic androgenic steroids at least once, and they are the seventh most commonly used drug in the country,' he added.

This study examined whether anabolic androgenic steroids could be associated with early coronary artery disease. It also tested whether reduced high-density lipoprotein (HDL) function could be a mechanism leading to coronary artery disease in anabolic androgenic steroid users.

The study included 51 men with an average age of 29 years (range 23–43 years). Of those, 21 did weight lifting and had taken anabolic androgenic steroids for at least two years, 20 did weight lifting but did not take steroids, and 10 were healthy but sedentary.

Participants underwent computed tomography coronary angiography to assess the presence of atherosclerosis in the coronary arteries. A urine test was performed in all participants to confirm steroid use. Blood samples were taken to measure lipid levels including HDL. The researchers used cell cultures to measure the ability of each participant's HDL to perform its normal function of removing cholesterol from macrophages.

The researchers found that 24% of steroid users had atherosclerosis in their coronary arteries, compared to none of the non-users and sedentary participants. The steroid users with atherosclerosis also had significantly reduced HDL levels and HDL function.

Mr Ribeiro de Souza said: 'Our study suggests that anabolic androgenic steroid use may be associated with the development of coronary artery disease in apparently healthy young people. Steroids may have an impact on the ability of HDL to remove cholesterol from macrophages, thereby promoting atherosclerosis.'

'This was a small, observational study and we cannot conclude that steroids cause atherosclerosis,' he continued. 'Larger studies with longer follow up are needed to confirm these results.'

Mr Ribeiro de Souza concluded: 'We observed coronary atherosclerosis in young anabolic androgenic steroid users, which in combination with lower HDL levels and reduced HDL function could increase the risk of cardiovascular events. Greater awareness is needed of the potential risks of these drugs.'

Dr Raul Santos, scientific chair of SBC 2017, said: 'This study, despite its small sample size, is well done and calls attention to a possible important health problem in Brazil and elsewhere since it shows not only the classic lipid disturbances induced by steroids but actually associates them with the subclinical presence of atherosclerosis, something that we are not supposed to find in young individuals.'

Prof Fausto Pinto, ESC immediate past president and course director of the ESC programme in Brazil, said: 'This is an important issue in cardiovascular prevention that deserves further study.

Role of melatonin in glucose uptake by cardiomyocytes from insulin-resistant Wistar rats

FREDERIC NDUHIRABANDI, BARBARA HUISAMEN, HANS STRIJDOM, AMANDA LOCHNER

Abstract

Aim: **Melatonin supplementation reduces insulin resistance and protects the heart in obese rats. However, its role in myocardial glucose uptake remains unknown. This study investigated the effect of short-term melatonin treatment on glucose uptake by cardiomyocytes isolated from obese and insulin-resistant rats.**

Methods: **Cardiomyocytes were isolated from obese rats fed a high-calorie diet for 16 to 23 weeks, their age-matched controls, as well as young control rats aged four to eight weeks. After incubation with melatonin with or without insulin, glucose uptake was initiated by the addition of 2-deoxy-D-[3H] glucose and measured after 30 minutes. Additional control and obese rats received melatonin in the drinking water (4 mg/kg/day) for the last six weeks of feeding (20 weeks) and glucose uptake was determined in isolated cardiomyocytes after incubation with insulin. Intraperitoneal glucose tolerance and biometric parameters were also measured.**

Results: **Obese rats (fed for more than 20 weeks) developed glucose intolerance. Cardiomyocytes isolated from these obese rats had a reduced response to insulin-stimulated glucose uptake (ISGU) ($p < 0.05$). Melatonin administration *in vitro* had no effect on glucose uptake per se. However, it increased ISGU by cardiomyocytes from the young rats ($p < 0.05$), while having no effect on ISGU by cardiomyocytes from the older control and obese groups. Melatonin *in vivo* had no significant effect on glucose tolerance, but it increased basal ($p < 0.05$) and ISGU by cardiomyocytes from the obese rats (50.1 ± 1.7 vs 32.1 ± 5.1 pmol/mg protein/30 min, $p < 0.01$).**

Conclusion: **These data suggest that short-term melatonin treatment *in vivo* but not *in vitro* improved glucose uptake and insulin responsiveness of cardiomyocytes in obesity and insulin-resistance states.**

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Although food shortage and malnutrition are still endemic in low- and middle-income countries,[1] excessive food intake and reduced physical activity associated with modern lifestyles, as well as night shift-work have led to a dramatic increase in the worldwide prevalence of obesity.[2,3] This is accompanied by various metabolic disorders including, among others, type 2 diabetes and cardiovascular diseases.[4,5] The major basis for this association is the well-known insulin resistance, which is a fundamental aspect in the development of type 2 diabetes and a common pathological link between obesity and cardiac diseases.[6-8] In this condition, the body produces insulin but does not use it properly due to decreased cellular sensitivity to its effect on uptake, metabolism and storage of glucose.[9]

Melatonin or N-acetyl-5-methoxytryptamine is the hormone secreted mainly by the pineal gland during the night. Its role in metabolic diseases has recently attracted many investigators.[10] Several animal[11-15] and epidemiological[16-20] studies support the role of melatonin in the regulation of glucose homeostasis. Low melatonin secretion levels are associated with elevated risk for hyperglycaemia and type 2 diabetes.[12,18] Importantly, removal of the melatonin receptor (MT1) significantly impairs the ability of mice to metabolise glucose and induces insulin resistance in these animals,[14] while melatonin administration improves glucose homeostasis in insulin-resistant animals.[11,13,21-24] However, the mechanism underlying the role of melatonin in glucose homeostasis is complex and not well understood.[25]

Impairment of insulin-stimulated glucose uptake is considered the most consistent change that develops early in the hearts of animal models of insulin resistance.[26] This change occurs as a consequence of both reduced glucose transporter 4 (GLUT4) protein expression and impaired translocation.[27] In this regard, while melatonin's effects have been extensively reported in other insulin-sensitive organs, such as the hypothalamus, skeletal muscle, liver and adipose tissue,[25,28-30] it is unclear whether melatonin affects cardiac glucose uptake in the insulin-resistant state.

A previous study showed that melatonin treatment was able to protect the heart against oxidative damage and restore the expression of the GLUT4 gene as well as glucose uptake of cardiomyocytes isolated from hyperthyroid rats,[31] supporting the ability of melatonin to improve changes in glucose uptake. Chronic melatonin administration given from the onset of the obesity-inducing diet was recently shown to prevent the harmful effects of obesity, such as insulin resistance and dyslipidaemia and to protect the hearts of obese rats against myocardial ischaemia–reperfusion injury.[32] In addition, we observed that short-term melatonin consumption also reduced systemic insulin resistance and conferred cardioprotection.[33] However, whether melatonin treatment affects myocardial insulin sensitivity and glucose uptake remains unknown.

The aim of this study was therefore to investigate the effect of melatonin treatment on myocardial glucose uptake using cardiomyocytes isolated from insulin-resistant rats and their aged-matched controls. To investigate whether melatonin has a direct effect on myocardial glucose uptake, melatonin was administered *in vitro* to isolated cardiomyocytes and *in vivo* for the measurement of glucose uptake. To evaluate the effect of ageing, cardiomyocytes isolated from normal control rats (seven to eight weeks old) were also included.

Methods

Sixty male Wistar rats were obtained from the University of Stellenbosch Central Research Facility. They were housed with free access to water and food and a 12-hour dark/light cycle (light from 06:00 to 18:00) with temperature and humidity kept constant at 22°C and 40%, respectively.

The experimental procedure was assessed and approved by the Committee for Ethical Animal Research of the Faculty of Medicine and Health Sciences, University of Stellenbosch (ethical clearance no P08/05/008). Animals were treated according to the *Guide for the Care and Use of Laboratory Animals* published by the US National Institutes of Health (NIH publication No 85–23, revised 1985) and the revised *South African National Standard for the Care and Use of Animals for Scientific Purposes* (South African Bureau of Standards, SANS 10386, 2008).

For evaluation of insulin responsiveness and sensitivity, cardiomyocytes were isolated from (1) normal rats (225–250 g) (n = 12) or (2) diet-induced obese rats (group D) (n = 24) and their age-matched controls (group C) (n = 24) fed a high-calorie diet and standard rat chow, respectively. The high-calorie diet consisted of 65% carbohydrates, 19% protein and 16% fat, while the standard rat chow consisted of 60% carbohydrate, 30% protein and 10% fat.[32] The diet-induced obese and age-matched control rats were seven to eight weeks old at the onset of the experimental programme, which was continued for a period of 16 to 23 weeks. To evaluate the progressive changes in insulin sensitivity, the feeding regime of our existing model of dietinduced obesity and insulin resistance[32] was varied from 16 to 23 weeks to exacerbate the effects of obesity, as previously reported.[33]

To determine whether short-term melatonin administration *in vitro* had a direct effect on myocardial glucose uptake, melatonin was administered to the cardiomyocytes after isolation (see below for cardiomyocyte preparation). Briefly, isolated cardiomyocytes were incubated with phloretin (glucose-uptake inhibitor, 400 µM), and melatonin (100 nM) with or without insulin (1–100 nM). Fresh melatonin (Sigma-Aldrich, St Louis, MO, USA) solution was used; melatonin was dissolved in a small quantity of ethanol and then in medium buffer to yield a final concentration of 1 nM, 10 nM, 100 nM, 1 µM or 10 µM (with < 0.005% ethanol). Ethanol at that concentration had no effect on glucose uptake by the cardiomyocytes (results not shown). Phloretin (Sigma-Aldrich, St Louis, MO, USA) was dissolved in dimethyl sulfoxide (DMSO), stored at –80°C as stock, and diluted with medium buffer immediately before use.

To evaluate the effect of *in vivo* melatonin treatment on myocardial glucose uptake, only rats fed for 20 weeks were used. While studying the effect of *in vitro* melatonin treatment, we observed that compared to their age-matched control rats, only cardiomyocytes isolated from obese rats fed for more than 20 weeks showed a significant decrease in insulin-stimulated glucose uptake (Fig. 3). Four groups were studied including: (1) untreated control (C), (2) treated control (CM), (3) untreated diet (D), and (4) treated diet (DM).

Melatonin was orally administered in the drinking water (4 mg/kg/day) for six weeks starting from the 14th week of feeding, a described previously.[32,33] This is the lowest concentration to have a significant effect in our model of diet-induced obesity.[33] Drinking water with or without melatonin was replaced every day one hour before lights off (18:00) and was available throughout the light and dark cycles.[33] In contrast to humans, rats are active during the night, when their blood melatonin levels are high. A period of six weeks has been shown as the shortest to elicit marked effects of melatonin on the hearts from diet-induced obese rats and to reverse several of the harmful effects of obesity.[33]

Animals were anaesthetised with sodium pentobarbitone (160 mg/kg, intraperitoneally). The hearts were immediately removed and perfused for isolation of cardiomyocytes, as described previously.[34] The body weight and visceral fat mass were recorded. Adiposity index was calculated as the ratio of visceral fat mass to body weight, multiplied by 100.[33]

Blood glucose levels were determined in the fasting state, as described previously,[35] at the same time (10:00–12:00). Blood was obtained via a tail prick and levels were determined using a conventional glucometer (Cipla MedPro, Bellville, South Africa). Intraperitoneal glucose tolerance (IPGT) curves were generated in animals after an overnight fasting period. Animals were injected with 1 g/kg of a 50% sucrose solution and blood glucose levels were recorded over a two-hour period.

Calcium-tolerant adult ventricular myocytes were isolated from the different animal groups, as previously reported.[34] After isolation, the myocytes were suspended in a medium buffer containing (in mM): HEPES 10, KCl 6, NaH_2PO_4 0.2, Na_2HPO_4 1, $MgSO_4$ 1.4, NaCl 128, pyruvate 2, glucose 5.5, and 2% BSA (fraction V, fatty acid free) plus calcium 1.25 mM, at pH 7.4. The cells were left for one to two hours under an oxygen atmosphere on a gently shaking platform to recover from the trauma of isolation. After recovery, the cells were allowed to settle into a loose pellet and the supernatant was removed. This procedure routinely rendered in excess of 80% viable cells, as measured by trypan blue exclusion. They were additionally washed twice with and suspended in a suitable volume of the above medium buffer but without glucose and pyruvate for subsequent glucose uptake determinations.

Cardiomyocyte glucose uptake was measured essentially as described previously[34] in a final assay volume of 750 µl. Cells prepared from the different groups of animals were incubated with or without one, 10 or 100 nM insulin for 30 minutes. After a total incubation period of 45 minutes, glucose uptake was initiated by addition of 2-deoxy-D-[3H] glucose (2DG) (1.5 µCi/ ml; final concentration 1.8 µM) (Perkin Elmer, Boston, USA).

Glucose uptake was allowed to progress for 30 minutes before stopping the reaction by adding phloretin (final concentration 400 µM). Thereafter, the cells were centrifuged at 1 000 g for one minute and the supernatant containing radiolabelled 2DG was aspirated. The subsequent pellet was washed twice with medium buffer without substrate and then dissolved in 0.5 M NaOH; 50 µl of this solution was used for the determination of the protein content by the method of Lowry *et al*.,[36] while the rest was counted for radioactivity using a scintillation counter (Beckman).

The Western blot technique was performed as previously reported,

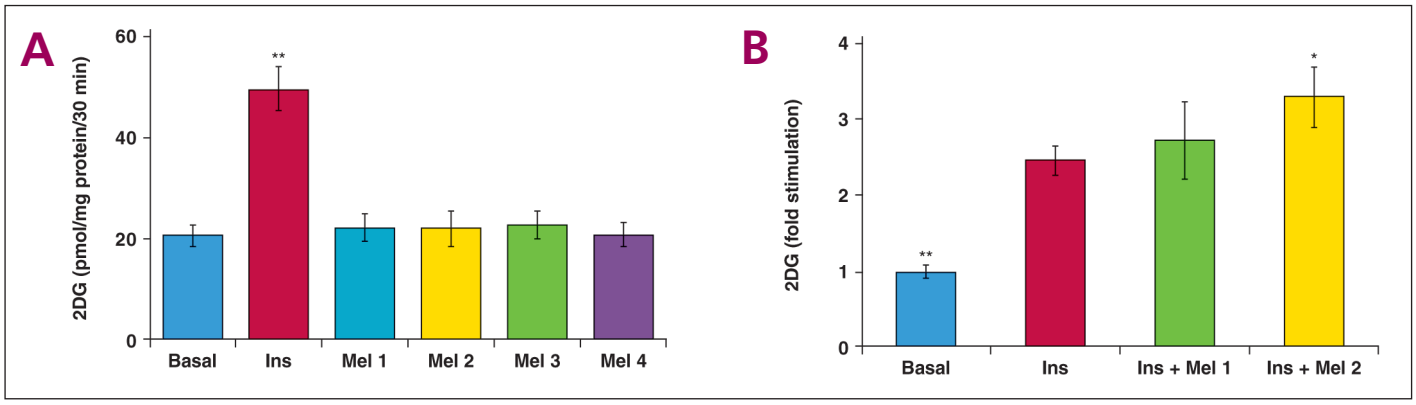

Figure 1. Effect of *in vitro* melatonin treatment on basal and insulin-stimulated glucose uptake by cardiomyocytes from young control rats (dose response). Cardiomyocytes were isolated and incubated with melatonin and/or insulin for a period of 30 minutes. The accumulated radiolabelled 2 deoxyglucose (2DG) was measured using a scintillation counter and expressed as pmol/mg protein/30 min. A: Effect on basal glucose uptake. Ins: insulin (1 nM), Mel: melatonin (Mel 1: 10 nM, Mel 2: 100 nM, Mel 3: 10 µM, Mel4: 50 µM), $^{**}p < 0.01$ (vs basal or melatonin), *n* (individual preparations): *n* = 12 (basal), 11 (Ins), three (Mel 1), eight (Mel 2), four (Mel 3), three (Mel 4); analysed in duplicate. B: Effect on insulin-stimulated glucose uptake (fold stimulation). Ins: insulin (1 nM), Mel: melatonin (Mel 1: 10 nM, Mel2: 100 nM); $^{*}p < 0.05$ (Ins vs Ins + Mel 2); $^{**}p < 0.05$ (basal vs Ins or Ins + Mel 1 or 2); *n* = 12 (basal), 11 (Ins), five (Ins + Mel 1), six (Ins + Mel 2) individual preparations/group; analysed in duplicate.

using the whole heart tissue[33] and isolated cardiomyocytes.[34] Cell lysates were made after 30 minutes' incubation with or without insulin or melatonin (before the addition of 2DG). Thereafter the cells were put on ice, transferred to Eppendorf tubes, quickly centrifuged and washed three times with ice-cold medium buffer without substrate. The resultant cell pellet was then lysed in 100 µl of lysis buffer.[34] At this point the cells were sonicated on ice (three times, intervals of three-second pulses with one-second break) and centrifuged for 20 minutes. The subsequent pellet was discarded and the supernatant used as cell lysate for Western blotting.

Total and phospho PKB/Akt (Ser-473) expressions were evaluated in the cardiomyocytes after incubation with melatonin with or without insulin, as previously described.[34] In addition, GLUT4 expression was evaluated in whole heart lysates after six weeks of melatonin treatment, as previously described.[33] All antibodies were purchased from Cell Signaling (USA). Beta-tubulin was used as a loading control. Protein activation is expressed in arbitrary densitometry units as phospho/total ratios.

Statistical analysis

Data are expressed as mean ± standard error of the mean (SEM). When comparisons between two groups (treated and untreated) were made, an unpaired Student's t-test was performed. For multiple comparisons, the ANOVA (two-way when appropriate), followed by the Bonferroni correction was applied. Statistical significance was considered for a *p*-value < 0.05.

Results

Effect of melatonin treatment in vitro *on glucose uptake by cardiomyocytes*

Compared to basal levels, melatonin treatment (10 and 100 nM, 10 and 50 µM) had no significant effect on glucose uptake by the cardiomyocytes isolated from normal rats (Fig. 1A). Insulin (1 nM) administration alone caused a 2.3-fold increase in glucose uptake compared to basal levels (Fig. 1B). However, when insulin was added to cells treated with melatonin (100 nM), there was a further stimulation of glucose uptake (3.4 ± 0.5- vs 2.5 ± 0.2-fold increase, $p < 0.05$) (Fig. 1B). As melatonin at other concentrations (10 nM) did not influence the levels of insulinstimulated glucose uptake (Fig. 1B) when compared to insulin alone, only 100 nM was used in subsequent experiments.

Cardiomyocytes isolated from the control (C) and obese (D) rats after 16 to 19 weeks of feeding, exhibited no significant difference in basal as well as insulin-stimulated glucose uptake between the two groups (Table 1, Fig. 2). As was observed in cardiomyocytes isolated from normal rats (Fig. 1A), melatonin administration (100 nM) also had no significant effect on basal glucose uptake in group C and D rats fed for 16 to 19 weeks (Table 1). However, it enhanced the insulin-stimulated glucose uptake in group C compared to group D rats (C: 73.9 ± 4.1 vs D: 47.5 ± 4.9 pmol/mg protein/30 min, $p < 0.05$) (Table 1, Fig. 2).

After 20 to 23 weeks of feeding, although the diet had no significant effect on basal glucose uptake by isolated cardiomyocytes

Table 1. Body weight and visceral mass of rats fed for 16 to 19 weeks and their corresponding glucose uptake by the cardiomyocytes

	Body weight and visceral fat mass			Glucose uptake (pmol/mg protein/30 min)			
Group	**Body weight (g)**	**Visceral fat (g)**	**Adiposity index**	**Basal**	**Insulin**	**Ins + Mel**	**Mel**
C	435 ± 21	17.0 ± 1.4	3.8 ± 0.18	25.6 ± 2.8	49.3 ± 5.6*	73.9 ± 4.1***#	25.5 ± 4.4
D	517 ± 11###	33.3 ± 1.3###	6.39 ± 0.3###	20.8 ± 3.1	40.8 ± 3.8*	47.5 ± 4.9*	20.0 ± 3.4
n	6	6	6	6	6	4	6

C: control, D: high-calorie diet, adiposity index = [(visceral fat/body weight) × 100], Ins: insulin (1 nM), Mel: melatonin (100 nM), $^{*}p < 0.05$ (vs basal), $^{***}p < 0.001$ (vs basal), #$p < 0.05$ (vs D), ###$p < 0.001$ (vs C), *n* = four to six individual preparations per group, uptake determined in duplicate for each preparation

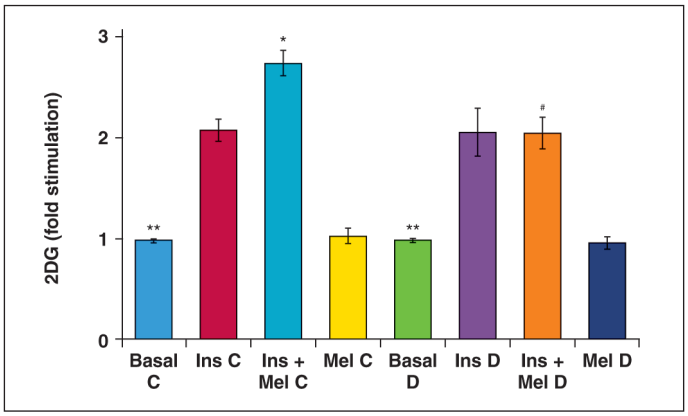

Figure 2. Effect of *in vitro* melatonin treatment on insulin-stimulated glucose uptake of cardiomyocytes isolated from control (C) and high-calorie diet (diet-induced obesity) (D) groups after 16 to 19 weeks. 2DG: 2 deoxyglucose, Ins: insulin (1 nM), Mel: melatonin (100 nM); *$p < 0.05$ (Ins C vs Ins + Mel C), **$p < 0.01$(basal vs Ins or Ins + Mel; Ins C vs Ins D), #$p < 0.05$ (Ins + Mel D vs Ins + Mel C), n = four to six individual preparations/group; analysed in duplicate.

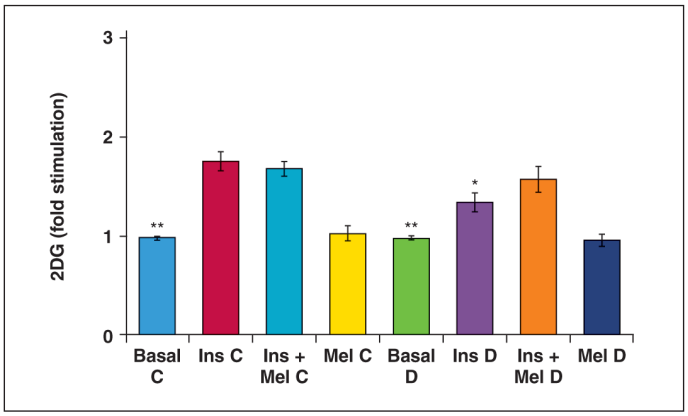

Figure 3. Effect of *in vitro* melatonin treatment on insulin-stimulated glucose uptake of cardiomyocytes isolated from control (C) and high-calorie diet (diet-induced obesity) (D) groups after 20 to 23 weeks. 2DG: 2 deoxyglucose, Ins: insulin (1 nM), Mel: melatonin (100 nM); *$p < 0.05$ (Ins C vs Ins D), **$p < 0.01$ (basal vs Ins or Ins + Mel), n = four to six individual preparations/group; analysed in duplicate.

(Table 2), insulin-stimulated glucose uptake was significantly lower in group D rats compared with the control group (C: 35.3 ± 6.3 vs D: 25.9 ± 1.6 pmol/mg protein/30 min, $p < 0.05$) (Fig. 3), while melatonin treatment had no effect on insulinstimulated glucose uptake in both group C and D rats (Fig. 3).

Effect of melatonin treatment in vivo *on glucose uptake by insulin-resistant cardiomyocytes*

After 20 to 23 weeks, rats fed a high-calorie diet exhibited significantly increased body weight (C: 433 ± 25 vs D: 538 ± 43 g, $p < 0.05$), visceral fat mass (C: 17.7 ± 1.8 vs D: 37.5 ± 7.5 g, $p < 0.001$) as well as adiposity index (Table 3). Melatonin treatment for six weeks reduced body weight and adiposity index values in group D rats ($p < 0.05$) (Table 3).

To evaluate the glucose uptake by cardiomyocytes from control and obese rats, a dose response with increasing concentrations of insulin was performed (Fig. 4). The diet had no effect on basal glucose uptake by cardiomyocytes isolated from both group C and D rats (Fig. 4). However it reduced insulin-stimulated glucose uptake in group D rats (Fig. 4, Table 2). Oral melatonin treatment *in vivo* for six weeks increased the basal glucose uptake by cardiomyocytes from group D rats (DM: 26.4 ± 2.1 vs D: 19.8 ± 3.4 pmol/mg protein/30 min, $p < 0.05$) while having no effect in group C rats (CM: 22.6 ± 3.7 vs C: 21.1 ± 3.5 pmol/mg protein/30 min, $p > 0.05$) (Fig. 4). Additionally, compared to their respective untreated group, cardiomyocytes isolated from the control treatment group (CM) had elevated insulin-stimulated glucose uptake ($p < 0.05$) (Fig. 4). Furthermore, cardiomyocytes from the D treatment group (DM) also showed a further elevation of insulin-stimulated glucose uptake with insulin administration (100 nM), compared to the untreated group (DM: 50.1 ± 1.7 vs D: 32.1 ± 5.1 pmol/mg protein/30 min, $p < 0.01$) (Fig. 4).

Effect of melatonin treatment in vivo *on IPGT test in insulin-resistant rats*

A high-calorie diet increased basal fasting blood glucose levels compared to the control diet (5.2 ± 0.28 vs 6.4 ± 0.17 mM, $p < 0.05$). Similarly, at the end of the test, group D rats continued to have elevated glucose levels (4.5 ± 0.2 vs 5.2 ± 0.1 mM, $p < 0.05$), compared to the control group (Fig. 5). The area under the curve was also elevated in group D rats, compared to the controls (870.7 ± 25.6 vs 761.8 ± 27.7, $p < 0.05$) (Table 3). However, despite a significant decrease in blood glucose levels in the melatonin-treated

Table 3. Body weight, visceral fat mass

Parameters	C	CM	D	DM
BBody weight (g)	433 ± 25	411 ± 17	538 ± 43***	488 ± 21#
Visceral fat (g)	17.7 ± 1.8	14.33 ± 1.9*	37.50 ± 7.5***	28 ± 4#
Adiposity index	4.1 ± 0.2	3.4 ± 0.16*	6.9 ± 0.23***	5.7 ± 0.3#
AUC for IPGT	761.5 ± 27.7	760.2 ± 38.8	870.7 ± 25.2*	826.7 ± 32.5
n	6	6	6	6

C: control, D: high-calorie diet, CM and DM: control and diet receiving melatonin for six weeks, adiposity index [(visceral fat/body weight) × 100], AUC: area under the curve, IPGT: intraperitoneal glucose tolerance, *$p < 0.05$ (vs C), ***$p < 0.001$(vs C), #$p < 0.05$ (vs D), n = six per group.

Table 2. Body weight and visceral mass of rats fed for 20 to 23 weeks and their corresponding glucose uptake by the cardiomyocytes

	Body weight and visceral fat mass			Glucose uptake (pmol/mg protein/30 min)			
Group	Body weight (g)	Visceral fat (g)	Adiposity index	Basal	Insulin	Ins + Mel	Mel
C	457 ± 14	18.4 ± 10.9	4 ± 0.2	19.9 ± 2.6**	35.3 ± 6.3#	33.5 ± 5.9	19.2 ± 1.7
D	575 ± 61###	38.7 ± 2.6###	6.7 ± 0.6###	18.1 ± 1.6**	25.9 ± 1.6	27.8 ± 1.1	18.4 ± 2.3
n	6	6	6	6	6	5	6

C: control, D: high-calorie diet, adiposity index [(visceral fat/body weight) × 100], Ins: insulin (1 nM), Mel: melatonin (100 nM), **$p < 0.01$ (vs Ins or Ins + Mel), #$p < 0.05$ (vs D), ###$p < 0.001$ (vs C), n = five to six individual preparations per group, uptake determined in duplicate for each preparation.

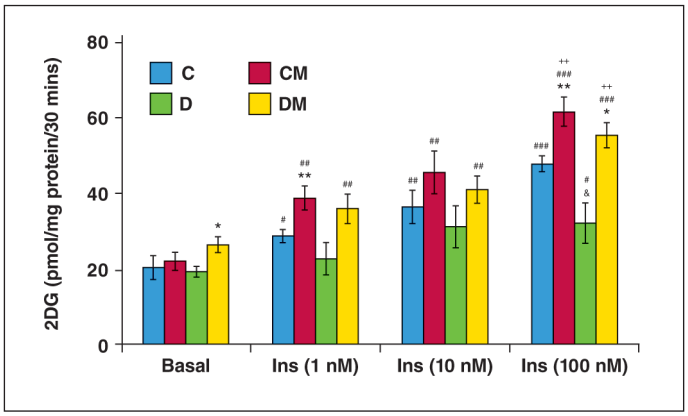

Figure 4. Effect of *in vivo* melatonin treatment (for the last six weeks of feeding) on insulin-stimulated glucose uptake by cardiomyocytes isolated from rats fed a high-calorie diet (20 weeks). Cardiomyocytes were isolated and stimulated with increasing concentrations of insulin for a period of 30 minutes. The accumulated radiolabelled 2DG was measured and expressed as pmol/mg protein/ 30 min. Ins: insulin, C: control, CM: control with melatonin, D: high-calorie diet (dietinduced obesity), DM: diet with melatonin. Treated vs untreated (same dose of insulin or basal): $*p < 0.05$ (DM vs D), $**p < 0.01$ (CM vs C). Different doses of insulin vs basal (same group of treatment): $^{\#}p < 0.05$ vs basal, $^{\#\#}p < 0.01$ vs basal, $^{\#\#\#}p < 0.001$ vs basal. C vs D (same dose of insulin): and $p < 0.05$ (D vs C). Comparison between different doses of insulin (same group of treatment): $^{++}p < 0.01$ vs 1 nM Ins, n = four to six individual preparations/group; analysed in duplicate.

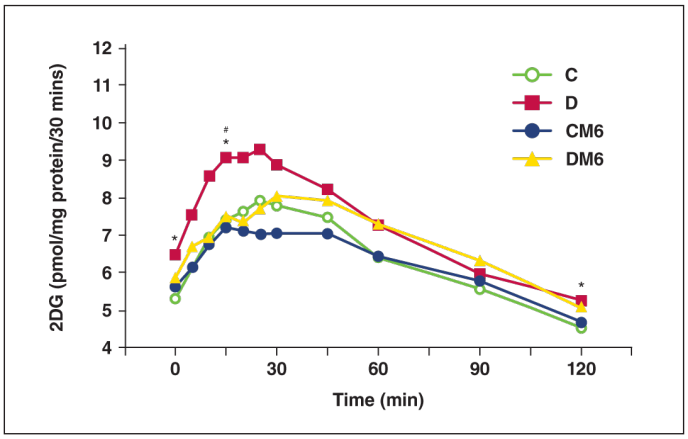

Figure 5. Effect of *in vivo* melatonin treatment (for the last six weeks of feeding) on intraperitoneal glucose tolerance. C: control, CM6: control with six weeks' melatonin treatment, D: high-calorie diet (diet-induced obesity), DM6: high-calorie diet with six weeks' melatonin treatment, $*p < 0.05$ (D vs C), $^{\#}p < 0.05$ (D vs DM6), n = six per group.

D rats observed between 15 and 25 minutes of the test, we noted that melatonin treatment had no significant effect on basal glucose levels and the overall area under curve in both groups (Fig. 5).

Discussion

Our aim was to investigate the effect of melatonin treatment on basal glucose uptake and insulin responsiveness as indicated by glucose uptake, using cardiomyocytes isolated from young control rats, age-matched controls and obese, insulin-resistant rats. The results indicated that (1) melatonin treatment *in vitro* had no effect on glucose uptake but increased insulin-stimulated glucose uptake by cardiomyocytes from only the young and age-matched control rats (Fig. 1B, Table 1); (2) melatonin treatment *in vivo* increased basal and insulin-stimulated glucose uptake by cardiomyocytes isolated from the hearts of obese, insulin-resistant rats.

During the basal state, glucose transport is commonly considered the rate-limiting step for muscle glucose metabolism.[37] The involvement of melatonin in glucose uptake was supported by the observation that pinealectomised animals develop insulin resistance associated with a decrease in glucose uptake by adipose tissue.[15,38] Accordingly, administration of melatonin reversed pinealectomy-induced insulin resistance and improved glucose uptake by isolated adipose tissue.[15,38] In contrast to this, our data show that melatonin per se had no significant effect on *in vitro* glucose uptake by cardiomyocytes isolated from young normal or obese rats and their age-matched controls (Fig. 1A, Tables 1, 2). A similar observation was previously reported in rat skeletal muscle cells[39] and chick brain,[40] as well as in adipose tissue from a female fruit bat.[41]

Of interest was our finding that acute melatonin administration *in vitro* enhanced insulin-stimulated glucose uptake by cardiomyocytes from normal young rats (Fig 1B) as well as the control rats fed for 16 to 19 weeks (Fig. 2). The enhanced insulin responsiveness of glucose uptake may be related to a synergistic interaction between melatonin and insulin action, supporting the insulin-sensitising effect by melatonin, as previously demonstrated.[39,41,42]

The *in vitro* melatonin-enhancing effect on insulin-stimulated glucose uptake was not observed in cardiomyocytes isolated from either the control or obese groups fed for more than 20 weeks (Fig. 3), indicating a progressive loss of the synergistic interaction between melatonin and insulin action. Although this is difficult to explain, it may have resulted from ageing in the control group, as previously demonstrated.[43] On the other hand, cardiomyocytes from obese animals fed for 16 to 19 weeks were almost as insulin-responsive as the control cardiac myocytes, but did not exhibit the potentiating effect of melatonin compared to the control group.

Various physiological factors such as an effect on adiponectin and leptin may have contributed to the overall effect of *in vivo* melatonin on glucose uptake, as previously discussed.[10] In a preventative-treatment setting, 16 weeks of melatonin consumption, starting before the establishment of obesity, reduced hypertriglyceridaemia and increased high-density lipoprotein cholesterol levels in rats fed the same high-calorie diet.[32] However, the exact mechanism whereby *in vivo* melatonin treatment affects glucose homeostasis and enhances insulin responsiveness is complex and not fully elucidated.

Melatonin induced a significant reduction in body weight, associated with a concomitant increase in basal glucose uptake by isolated cardiomyocytes from the obese rats. This effect is consistent with previous observations that chronic melatonin treatment reduced body weight gain and insulin resistance in mice[11] and rats[21] fed a high-fat diet, as well as in old obese[28] and young Zucker diabetic fatty[13] rats. Therefore, melatonin action may involve melatonin receptors and various indirect effects on the liver, pancreas and other peripheral insulin-sensitive organs, such as adipose tissue and skeletal muscle.[25] A recent report shows that the removal of melatonin receptors (MT1 or MT2) in mice abolished the daily rhythm in blood glucose levels,[44] confirming the role of melatonin signalling in the control of glucose homeostasis.

Contrary to the *in vitro* situation, melatonin administered *in vivo* increased basal glucose uptake by cardiomyocytes isolated from obese rats. Mechanistically, this may involve glucose transporter 1 (GLUT1), which is usually associated with basal glucose uptake

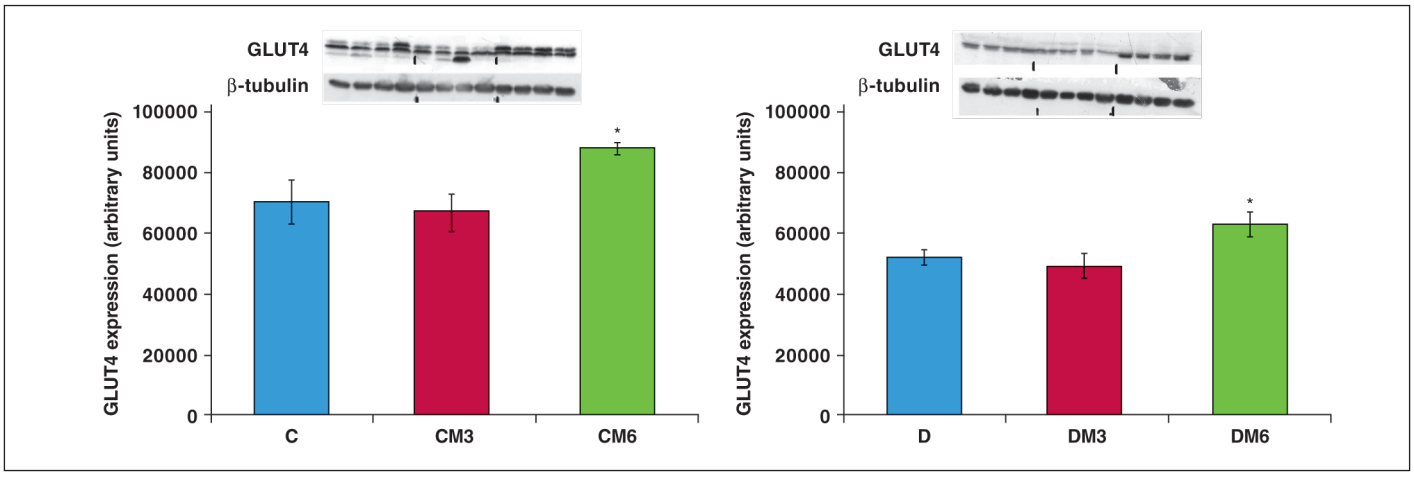

Figure 6. The effects of melatonin treatment on GLUT4 expression after three and six weeks of treatment. Hearts were isolated from rats fed a high-calorie diet for 20 weeks and their age-matched controls. Both control and obese groups received drinking water with/without melatonin (4 mg/kg/day) for three or six weeks starting after 14 weeks of feeding. C: control group, D: highcalorie diet (obesity) group; CM3, DM3, CM6 and DM6: group C and D rats receiving melatonin treatment for three weeks (M3) or six weeks (M6); beta-tubulin was used as a loading control. C and D performed on the different blot ($p > 0.05$ C vs D), *$p < 0.05$ (CM6 vs C) or DM6 vs D, n = four hearts/group.

by cardiomyocytes, and its expression would give more insight.[45] Therefore, it may be that there was an increase in the expression or membrane translocation of GLUT1 in these cardiomyocytes from obese rats treated with melatonin. In addition, insulin was able to elicit a significant response in untreated control animals, while this was not the case in the obese animals after 20 to 23 weeks. This observation could be explained by the insulin-resistant state of the cells from the obese animals compared to their controls. Interestingly, cardiomyocytes prepared from control as well as obese animals treated with melatonin showed a significantly higher response to insulin than the untreated counterparts (Fig. 4).

With regard to the effect of melatonin on glucose tolerance, the present data show that obese rats developed glucose intolerance, and melatonin had no effect on basal glucose levels (10:00–12:00). While data on nocturnal glucose levels may be different, six-week melatonin treatment also reduced systemic insulin resistance in obese rats without affecting basal fasting blood glucose levels.[33] These results are consistent with previous findings:[46] between 15 and 25 minutes following glucose injection, obese melatonin-treated rats had a significant decrease in blood glucose levels compared to the untreated obese group, somehow indicating their increased ability to absorb glucose.

The reduction in insulin resistance or improved glucose uptake and utilisation may involve changes in the metabolic profile, such as increasing adiponectin levels after long-[13,23] and short-term[33] melatonin administration. Melatonin-induced beneficial changes in adipose tissue[41,47] may in turn additionally contribute to improved whole-body insulin sensitivity. Moreover, as indicated above, melatonin may improve glucose homeostasis via its actions in the hypothalamus and liver.[48]

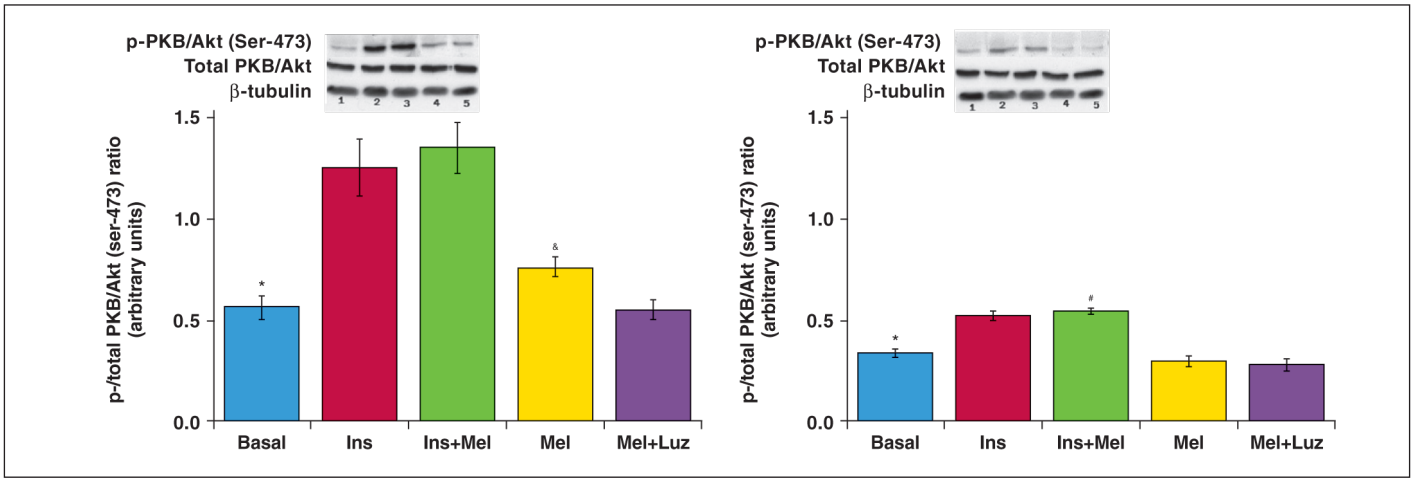

Figure 7. Effects of *in vitro* melatonin administration to isolated cardiomyocytes on PKB/Akt expression and phosphorylation (rats fed for 20 weeks). Cardiomyocytes were isolated and incubated with melatonin with or without insulin stimulation. C: control, D: high-calorie diet. 1: basal, 2: Ins (insulin), 3: Insulin + melatonin, 4: Mel (melatonin), 5: luzindole + melatonin, Luz (luzindole), C: *$p < 0.05$ (Ins or Ins + Mel vs basal), and $p < 0.05$ (Mel vs basal or Mel + Luz), D: *$p < 0.05$ (Ins or Ins + Mel vs basal), #$p < 0.05$ (D vs C), n = three individual preparations/group. Blots are representative. Beta-tubulin was used as a loading control. C and D performed on the same blot.

Impairment of insulin-stimulated glucose transport is considered the most consistent change that develops early in the hearts of animal models of insulin resistance.[26] Since GLUT4 is the most prominent glucose transporter in differentiated cardiomyocytes,[49] our data underscore the importance of further investigation analysing the expression of intermediates of insulin signal transduction and the effects of melatonin treatment thereupon in cardiomyocytes isolated from treated control and obese hearts.

The effect of six weeks of melatonin treatment on the basal expression and activation of a number of intermediates in myocardial tissue from control and obese rats has been studied previously in our laboratory: baseline activation of PKB/ Akt, extracellular signal-regulated kinase (ERK) p42/p44 and glycogen synthase kinase 3 beta (GSK3β) were found to be significantly upregulated by melatonin treatment in both control and obese rats.[33] However, it will be also important to determine whether these observed beneficial changes were secondary to the improved whole-body insulin sensitivity or whether there were changes in cardiomyocyte protein expression and activation per se elicited by melatonin treatment.

In this regard, a marginal increase in GLUT4 expression was previously reported to be associated with an increase in glucose uptake by melatonin-treated adipose tissue.[41] Our additional observations showed significant increases in GLUT4 expression in the whole heart tissue of obese rats after six weeks of *in vivo* melatonin treatment (Fig. 6). Interestingly, as expected, the significant lowering in glucose uptake by cardiomyocytes from obese rats was also reflected in the reduction in PKB/Akt activation when compared with their age-matched controls (Fig. 7).

Conclusion

To our knowledge, this is the first study on the role of melatonin in cardiac glucose uptake in an insulin-resistant state. The cardiovascular benefits of melatonin supplementation are supported by the fact that circulating melatonin levels are decreased in cardiovascular diseases.[50,51] Convincing evidence exists for the benefits of increasing glucose uptake as an important therapeutic goal in the management of left ventricular systolic dysfunction.[52] Although its role in melatonin-induced cardioprotection needs further investigation, present data suggest that short-term melatonin treatment *in vivo*, but not *in vitro*, improved basal glucose uptake and insulin responsiveness in insulin-resistant cardiomyocytes isolated from obese rats.

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Daniel Binette: new managing director, Lilly South Africa

Daniel Binette – Managing Director, Lilly South Africa

Daniel Binette has been appointed managing director of Lilly South Africa. His career at Lilly Canada spans 17 years and he is known as a strategic and dynamic results-orientated leader with multiple launch experiences (Forteo, Cymbalta Pain, Cialis BPH and Axiron). Most recently, Daniel was next-generation customer engagement leader where he provided a strong understanding of external trends and potential innovative solutions to address customer needs. He is described as a driven, personable and innovative leader. He graduated from Laval University in Quebec, Canada where he holds an undergrad in Business Science and an MBA.

Prevalence of obesity and body size perceptions in urban and rural Senegal: new insight on the epidemiological transition in West Africa

ENGUERRAN MACIA, EMMANUEL COHEN, LAMINE GUEYE, GILLES BOETSCH, PRISCILLA DUBOZ

Abstract

Background: **The objectives of this study were to assess the prevalence of obesity in Dakar and in Tessekere, a rural municipality in northern Senegal, and to compare ideal body size between these populations.**

Methods: **A cross-sectional survey was carried out in 2015 on a representative sample of 1 000 adults, aged 20 years and older in Dakar, and 500 adults of the same age in Tessekere.**

Results: **The prevalence of obesity and overweight was higher in Dakar than in Tessekere. However, overweight and obesity rates of young women living in this rural area were close to those of young women in Dakar. At a body mass index of 27.5 kg/m², less than 40% of the men in Dakar and Tessekere found themselves too fat, compared to 50% of urban women and 30% of rural women.**

Conclusion: **This study explains how and why obesity is becoming a rural health problem in Senegal.**

Keywords: Africa, biological anthropology, epidemiological transition, nutrition transition, overweight

Overweight and obesity are important risk factors for cardiovascular disease.[1,2] The increasing prevalence of obesity during the last few decades in a number of countries[3] has been reported as a global pandemic and a major public health issue worldwide.[4-7] Sub-Saharan Africa (SSA) is not immune to this epidemic.[8,9] In urban West Africa, the prevalence of obesity more than doubled from 7.0% in 1990–94 to 15.0% in 2000–04.[10] However, over this 15-year period, Abubakari and colleagues noted that obesity rates seemed to remain unchanged in rural West Africa, possibly due to the small number of studies retrieved from these populations.[10]

Despite the threat posed by obesity in West Africa, there are very few studies addressing this issue in Senegal and none in the rural areas. To our knowledge, few studies have evaluated the prevalence of obesity among both men and women in Dakar,[11] the political and economic capital of the country. In terms of body mass index (BMI), the prevalence of overweight and general obesity in 2009 was 22.3 and 8.3%, respectively, in Dakar, whereas using waist circumference (WC), the prevalence of central obesity was 21.2%.[11] Only by monitoring prevalence over time can the evolution of the obesity epidemic in the Senegalese capital be understood.[1]

Various factors contribute to the high prevalence of obesity in SSA.[8,9] More precisely, numerous macrosocial (e.g. urbanisation,[12] globalisation[9]), genetic,[13] behavioural (mainly diet and physical activity[14]), sociodemographic,[15] and culturally underlying[16] factors have been reported as determinants of obesity in West Africa. In the context of this comparative urban–rural study in Senegal, a focus on urbanisation, sociodemographics and perception of body size is fundamental.

It is now well established that urbanisation is a major driving force in obesity, by reducing physical activity and increasing consumption of energy-dense diets.[17] In West Africa, urban residents have three times the odds of being obese than rural residents.[10] Among sociodemographic factors, age and gender have regularly been shown to be associated with obesity in SSA[8] and West Africa.[10]

Beyond these recurrent and robust predictors, the role of socioeconomic status (SES) seems more complex in SSA. Indeed, while studies regularly report that obesity is significantly more likely to occur in the highest SES group,[8] Ziraba and colleagues observed that the increase in obesity was higher among the poorest than among the richest African urban dwellers during the period 1995 to 2005.[18] In line with the epidemiological transition occurring in SSA,[19,20] the relationship between obesity and SES is likely to change in the coming years and gradually affect the lowest SES groups more than the highest.

In SSA, positive traditional representations of stoutness – the social validation of the big belly for men and large hips for women[21] – may also contribute to the gradual development of obesity. Obesity is a concept that is viewed differently across cultures.[22] In SSA, where HIV and other diseases associated with wasting away are prevalent, overweight and obesity have been associated with health.[16,23] Moreover, once married, extra weight is seen as an indicator that the spouse is well cared for.[24] In Pikine, a suburb of Dakar, these positive perceptions of stoutness have been observed among women.[25] However, no study has been conducted from this perspective among urban men, or among the rural population.

Therefore, the objectives of this study were (1) to assess and compare the prevalence of obesity, general and central, in Dakar and

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in Tessekere, a rural municipality in northern Senegal, and to analyse trends in obesity in Dakar; (2) to determine sociodemographic risk factors for obesity in both environments; and (3) to compare ideal body size between urban and rural areas.

Methods

The study was approved by the National Ethics Committee for Health Research of Senegal (protocol SEN13/67, no 0272). The research was conducted in accordance with the Declaration of Helsinki, and written informed consent was obtained from participants.

This study was conducted from February to August 2015 on a sample of 1 000 individuals, aged 20 years and older in Dakar, and on a sample of 500 adults of the same age bracket in the Tessekere municipality. The samples were constructed using the combined quota method (cross-section by age, gender and town of residence in Dakar; only by age and gender in Tessekere municipality) in order to strive for representativeness of the population aged 20 years and older living in the department of Dakar and in Tessekere municipality. Data from the Agence Nationale de la Statistique et de la Démographie dating from the last census (2013) were used.

The quota variables used were gender (male/female), age (20–29, 30–39, 40–49, 50–59, and 60 years and over, with an upper age limit of 100 years) and, for Dakar, town of residence. In Dakar, the towns were grouped by the four arrondissements making up the department: Plateau-Gorée (five towns), Grand Dakar (six towns), Parcelles Assainies (four towns) and Almadies (four towns). In practical terms, this method requires constructing a sample that reflects the proportions observed in each target population. For example, according to the last census, men aged 20–29 years living in the town of Medina (arrondissement of Plateau-Gorée) represented 1.9% of the population aged 20 years and over living in the department of Dakar. The sample was constructed to reflect this proportion and it included 19 men aged 20–29 living in this town.

Inclusion criteria were individuals 20 years old or older, living in the department of Dakar. Pregnant women were excluded from the study.

Eight trained investigators (PhD students in Medicine, Pharmacy and Sociology) started out each day from different points in each town (Dakar) or camp (Tessekere) to interview individuals in Wolof, Haalpulaar or French in every third home. Investigators had a certain number of individuals to interview to meet the quotas. Only one person was selected as a respondent in each home. Investigators went to the house, inquired about the inhabitants and then chose the first person they saw who met the characteristics needed for the quotas. In-person interviews were conducted. They ranged from 45 minutes to more than one hour and 30 minutes, depending on respondent availability and desire to talk.

Weight was measured using a digital scale (measurement accuracy of 100 g), with subjects dressed in minimal clothing and barefoot. To measure height, the subject was to stand 'at attention', arms at the sides, heels together, without shoes. Following World Health Organisation (WHO) recommendations, BMI was calculated by dividing the weight (kg) by the square of the height (m^2). Underweight was defined as BMI < 18.5 kg/m^2; overweight was defined as 25 ≤ BMI < 30 kg/m^2; and obesity corresponded to a BMI of ≥ 30 kg/m^2.[26]

Waist circumference (WC) was measured at the narrowest point of the abdomen at the end of a normal expiration. WC was measured using a measuring tape with 1-mm accuracy. WC of ≥ 102 cm in men and ≥ 88 cm in women was considered central obesity.[27] Waist-to-hip ratio (WHR) was also used as a criterion of central obesity: a WHR of ≥ 0.9 in men and ≥ 0.8 in women was considered central obesity.[28]

Among the sociodemographic data collected during the interviews, three variables were taken into account for this study: age, gender and educational level. Four age groups were defined: 20–29, 30–39, 40–49 and 50 years and over. Gender was coded as follows: 1 for women, 0 for men. In Dakar, five levels of education were defined based on the Senegalese school system: none, primary (one to five years of schooling), intermediate (six to eight years), secondary (nine to 12 years), and university (13 years and over). In the Tessekere municipality, given the large proportion of persons who have never attended school (76%), the educational level was dichotomised: no schooling/one or more years of schooling.

Satisfaction with body weight was assessed in one question, with five possible responses: 'Do you think you are: too thin, a little too thin, average, a little too fat, too fat?' To determine ideal body size, we took the BMI at which the same percentage of individuals believed they were too heavy as those who felt they were too thin.[29]

We also used the body size scale (BSS), developed and validated by Cohen *et al*. in Senegal,[30] to assess ideal body size (IBS) of women and men, to obtain a complementary representation of body image assessed from the questionnaire. This tool has two advantages: (1) it consists of a gender-specific scale of nine models; and (2) it represents real black models with their anthropometric characteristics to assess specific body weight perceptions in African populations. One model represents the underweight category, three models the normal-weight category, two models the overweight category, and one model each class of obesity level as defined by the WHO (30.0 < BMI ≤ 34.9 kg/m^2, 35.0 < BMI ≤ 39.9 kg/m^2, and ≥ 40 kg/m^2). BSS was considered a numerical variable, as each human picture ranged from 1 to 9 according to increasing BMI categories to measure ideal body size.

Statistical analysis

To answer our research questions, we used the Student's *t*-test, ANOVA, chi-squared test and logistic regressions. Results are expressed as mean ± standard deviation for continuous variables or as percentages for categorical variables. Bivariate comparisons were performed using the Student's *t*-test, ANOVA for continuous variables, and chi-squared tests for categorical variables. Multivariate analyses were performed using binary logistic regression and results are expressed as odds ratios with 95% confidence intervals (CIs). The software used for the statistical analysis was SPSS Statistics 22 for Windows.

Results

Among the 1 000 individuals included in the Dakar sample, 16 women were excluded because they reported pregnancy. Similarly, four women of the Tessekere sample were also excluded for pregnancy. Analyses were finally performed on a sample of 984 Dakarites and 496 Tessekere dwellers. The distributions of height, weight, BMI, WC, WHR, general and central obesity,

Table 1. Demographic and anthropomatic characteristics of the sample

	Dakar				Tessekere			
Characteristics	**Total (*n* = 984)**	**Male (*n* = 494)**	**Female (*n* = 490)**	***p*-value**	**Total (*n* = 496)**	**Male (*n* = 241)**	**Female (*n* = 255)**	***p*-value**
Age (years)	35.70 ± 13.16	35.89 ± 13.27	35.51 ± 13.07	0.652	37.33 ± 15.25	37.26 ± 15.45	37.40 ± 15.08	0.917
Height (cm)	172.56 ± 9.87	178.96 ± 8.07	166.11 ± 6.88	< 0.001	169.63 ± 10.38	175.85 ± 8.09	163.75 ± 8.77	< 0.001
Weight (kg)	69.28 ± 14.44	70.21 ± 16.67	68.34 ± 16.00	0.043	60.25 ± 12.32	62.38 ± 11.26	58.23 ± 12.96	< 0.001
BMI (kg/m²)	23.33 ± 4.89	21.91 ± 3.54	24.76 ± 5.59	< 0.001	20.97 ± 4.07	20.15 ± 3.24	21.74 ± 4.60	< 0.001
General obesity, *n* (%)	95 (9.7)	14 (2.8)	81 (16.5)	< 0.001	14 (2.8)	2 (0.8)	12 (4.7)	0.009
WC (cm)	84.31 ± 13.02	81.51 ± 10.65	87.14 ± 14.51	< 0.001	77.25 ± 10.59	76.13 ± 9.31	78.32 ± 11.59	0.021
Central obesity by WC, *n* (%)	256 (26)	21 (4.3)	235 (48)	< 0.001	59 (11.9)	3 (1.2)	56 (22.?)	< 0.001
WHR	0.836 ± 0.081	0.837 ± 0.069	0.834 ± 0.092	0.579	0.839 ± 0.079	0.847 ± 0.075	0.831 ± 0.082	0.019
Central obesity by WHR, n (%)	393 (39.9)	83 (16.8)	310 (63.3)	< 0.001	117 (23.6)	17 (7.1)	100 (39.2)	< 0.001
Educational level (Dakar/Tessekere), *n* (%)			< 0.001				0.006	
None/none	208 (21.1)	84 (27)	124 (25.3)		373 (75.2)	168 (69.7)	205 (80.4)	
Primary/1 year or +	348 (35.5)	163 (33)	185 (37.8)		123 (24.8)	73 (30.3)	50 (19.6)	
Intermediate	197 (20)	109 (22.1)	88 (18)					
Secondary	91 (9.2)	51 (10.3)	40 (8.2)					
University	140 (14.2)	87 (17.6)	53 (10.8)					

BMI: body mass index, WC: waist circumference, WHR: waist–hip ratio.

sociodemographic variables, and comparisons between males and females in both environments are summarised in Table 1. The results show that men and women differed for all the factors studied except for age in both environments, and for WHR in Dakar.

In Dakar, the prevalence of underweight, overweight and general obesity in terms of BMI was 12.6% (95% CI: 10.5–14.7), 19.2% (95% CI: 16.7–21.7) and 9.7% (95% CI: 7.9–11.5), respectively. The prevalence of central obesity was 26.0% (95% CI: 23.3–28.7) using WC, and 39.9% (95% CI: 36.8–43.0) using WHR (Table 2).

In Tessekere, the prevalence of underweight, overweight and general obesity in terms of BMI was 29.6% (95% CI: 25.6–33.6), 13.3% (95% CI: 10.3–16.3) and 2.8% (95% CI: 1.3–4.3), respectively. The prevalence of central obesity was 11.9% (95% CI: 9.1–14.7) using WC, and 23.6% (95% CI: 19.9–27.3) using WHR (Table 2).

Dakar residents were more often overweight and obese and less often thin than the Tessekere inhabitants [χ^2 (3 df) = 80.9; $p < 0.001$]. Likewise, they showed higher central obesity rates than the Tessekere inhabitants [WC: χ^2 (1 df) = 39.3, $p < 0.001$; WHR: χ^2 (1 df) = 39, $p < 0.001$].

In Dakar as in Tessekere, bivariate analyses showed that all the sociodemographic factors studied were associated with general and central obesity (Table 3). The prevalence of general and central obesity rose gradually with age in both environments, except for obesity based on WC in Tessekere, which reached its highest rate among people between the ages of 40 and 49 years.

Table 2. Prevalence (%) of underweight, overweight, general obesity and central obesity by place of residence

Criterion	Category	Dakar	Tessekere
BMI	Underweight	12.6 (10.5–14.7)	29.6 (25.6–33.6)
	Overweight	19.2 (16.7–21.7)	13.3 (10.3–16.3)
	General obesity	9.7 (7.9–11.5)	2.8 (1.3–4.3)
WC	Central obesity	26.0 (23.3–28.7)	11.9 (9.1–14.7)
WHR	Central obesity	39.9 (36.8–43.0)	23.6 (19.9–27.3)

BMI: body mass index, WC: waist circumference, WHR: waist-hip ratio.
In brackets: 95% confidence limits.

In the urban and rural areas studied, general obesity affected women six times more often than men, and their WC exceeded the threshold of obesity 11 times and 18 more often than men in Dakar and Tessekere, respectively.

As shown in Fig. 1, the prevalence of overweight/obesity (using BMI) rose with age among men and women in Dakar. The same pattern was observed among men in Tessekere. However, among rural women, the prevalence of overweight/obesity reached its highest rate between the ages of 30 and 39 years.

Multivariate analyses showed that age and gender were the primary risk factors for overweight/obesity in Dakar and Tessekere (Table 4). Educational level also showed significant associations with BMI ≥ 25 kg/m², but only in the urban area, where people with between one and eight years of schooling had greater chances of being overweight or obese than people who attended university. Gender was the primary risk factor for central obesity (WC and WHR) in both environments (Table 4).

In Dakar, 50% of the study participants were satisfied with their weight, 27% thought they were too thin and 23% too fat. Men were more often satisfied with their weight than women (57 vs 43%), who in turn more often thought themselves too heavy (33 vs

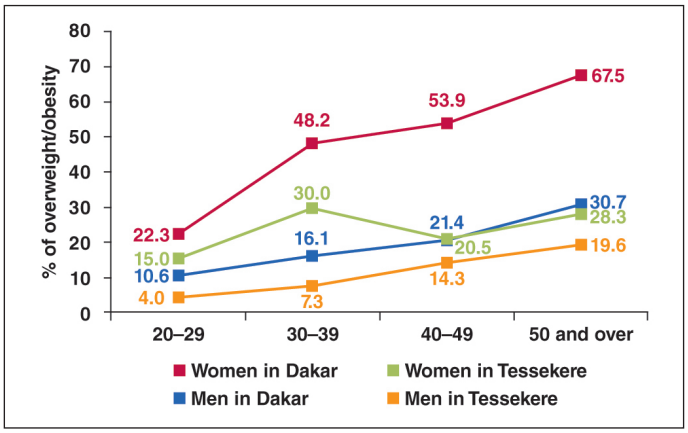

Figure 1. Age- and gender-specific prevalence (%) of overweight/obesity in Dakar and Tessekere.

Table 3. Prevalence (%) of underweight, overweight, obesity and central obesity by age, gender and educational level in Dakar and Tessekere

		Obesity based on BMI				Obesity based on WHR		Obesity based on WC	
Variable	***n***	**Underweight**	**Overweight**	**Obese**	***p*-value**	**Obese**	***p*-value**	**Obese**	***p*-value**
Dakar									
Age (years)									
20–29	413	18.6	12.8	3.6	< 0.001	26.2	< 0.001	12.6	< 0.001
30–39	266	11.3	22.6	9.8		37.6		25.9	
40–49	156	5.1	20.5	16.7		54.5		37.2	
≥ 50	149	6	29.5	18.8		67.1		51.7	
Gender									
Male	494	15.4	14	2.8	< 0.001	16.8	< 0.001	4.3	< 0.001
Female	490	9.8	24.5	16.5		63.3		48	
Educational level									
Illiterate	208	8.7	21.6	12	< 0.01	51.9	< 0.001	32.2	< 0.001
Primary	348	10.9	21.6	10.3		40.8		29.9	
Intermediate	197	13.2	20.8	10.2		35		25.4	
Secondary	91	19.8	15.4	9.9		41.8		25.3	
University	140	17.1	10	3.6		25.7		8.6	
Tessekere									
Age (years)									
20–29	200	33	9.5	0	< 0.01	14	< 0.001	4.5	< 0.001
30–39	115	30.4	17.4	1.7		20		9.6	
40–49	77	27.3	11.7	6.5		28.6		23.4	
≥ 50	104	24	17.3	6.7		42.3		20.2	
Gender									
Male	241	34.4	8.7	0.8	< 0.001	7.1	< 0.001	1.2	< 0.001
Female	255	25.1	17.6	4.7		39.2		22	
Educational level									
None	373	30.6	12.9	2.9	NS	26.5	< 0.01	13.1	NS
1 year and +	123	26.8	14.6	2.4		14.6		8.1	

BMI: body mass index, WC: waist circumference, WHR: waist-hip ratio.

13%; $p < 0.001$). In Tessekere, the majority found themselves too thin (53%), 8% believed they were too fat, and 39% were satisfied with their weight. Men were more often satisfied with their weight than women (45 vs 34%; $p < 0.01$).

Fig. 2 shows that ideal BMI for men and women in Dakar was found to be 23.5 kg/m². In Tessekere, ideal BMI for men was 25.5 kg/m². For women in this rural area, the tendency was not as clear, but the ideal BMI for rural women could nevertheless be situated in the overweight category. We should note that at a BMI of 27.5 kg/m², only 42% of the men in Dakar felt too fat, as opposed to 49% of the women. In Tessekere, for the same BMI, 41% of the men felt too heavy as opposed to only 30% of the women.

In Tessekere, 10 people were unable to judge ideal body size by the BSS. Analyses concerning this scale were therefore done on 486 participants in the rural area and 984 in the urban area (Fig. 3). First, we observed that for both male and female scales, averages of IBS for oneself and the opposite sex were lower in urban Senegalese than in rural Senegalese. The ideal male and female bodies fell within the normal range in Dakar, and in the overweight category in Tessekere. Second, there were no significant differences between men and women from each environment on each scale, except for the female scale in Dakar; urban women perceived the ideal female body size as heavier than their male counterparts ($t = 5.45$; $p < 0.001$).

Discussion

This study is to our knowledge the first to evaluate the prevalence of obesity among both men and women in urban and rural Senegal.

Table 4. Adjusted odds ratio (OR) for overweight/obesity and central obesity in Dakar ($n = 984$) and Tessekere ($n = 496$)

	Overweight/ obesity		Obesity based on WHR		Obesity based on WC	
Variable	***OR***	***95%* CI**	***OR***	***95%* CI**	**OR**	***95%* CI**
Dakar						
Age (20–29)						
30–39	2.39***	1.62–3.52	1.96**	1.32–2.92	2.89***	1.82–4.60
40–49	3.17***	2.03–4.95	5.34***	3.29–8.66	7.47***	4.24–13.18
≥ 50	5.38***	3.42–8.45	12.40***	7.35–20.93	29.51***	14.79–58.90
Gender (men)						
Women	3.85***	2.81–5.29	13.24***	9.21–19.05	49.33***	26.74–91.01
Educational level (university)						
None	1.47	0.80–2.72	1.23	0.70–2.18	1.43	0.65–3.16
Primary	1.85*	1.05–3.26	1.1	10.65–1.85	2.58*	1.24–5.40
Intermediate	1.96*	1.07–3.58	0.94	0.53–1.66	2.58*	1.17–5.68
Secondary	1.59	0.77–3.25	1.59	0.81–3.12	2.91*	1.17–7.21
Tessekere						
Age (20–29)						
30–39	2.35*	1.19–4.65	1.55	0.81–2.96	2.29	0.89–5.89
40–49	2.49*	1.13–5.46	2.53**	1.25–5.13	8.74***	3.34–22.83
≥ 50	3.89***	1.93–7.86	6.03***	3.13–11.60	7.67***	3.02–19.45
Gender (men)						
Women	2.93***	1.71–5.02	10.08***	5.59–18.18	27.16***	8.15–90.55
Educational level (1 year or +)						
None	0.57	0.31–1.05	1.07	0.57–2.00	0.56	0.23–1.34

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$. BMI: body mass index, WC: waist circumference, WHR: waist-hip ratio.

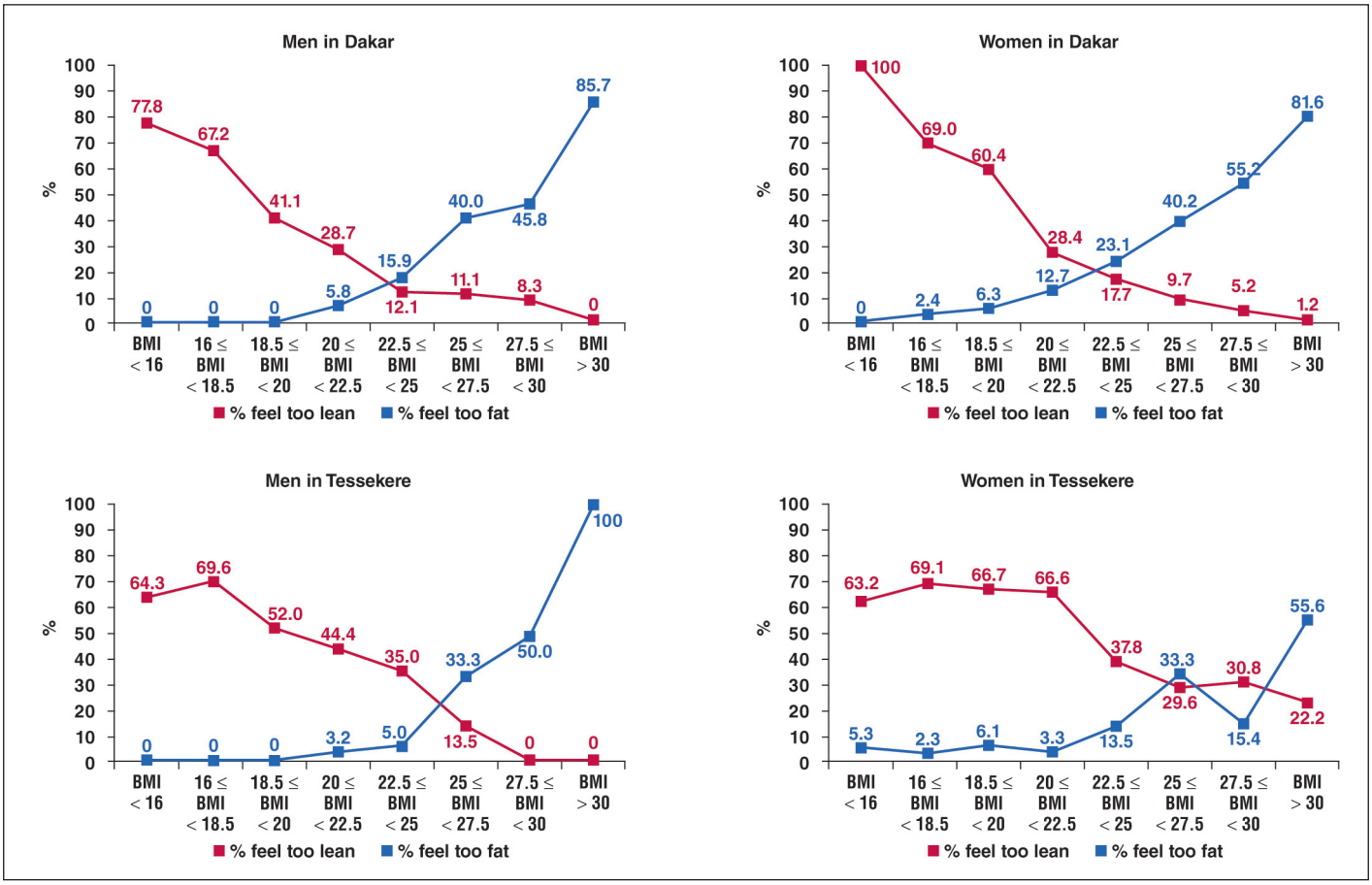

Figure 2. Satisfaction with weight by BMI among men and women in Dakar and Tessekere.

Moreover, it is also the first study to assess perception of body size in both genders in this country.

In Dakar, the prevalence of general obesity was 9.7%, and that of overweight, 19.2%. These prevalence rates place Dakar among the West African cities that are least affected by problems of excess weight.[31,32] Comparison of our results with those of a study carried out among men and women in Dakar in 2009[11] suggests that prevalence of general obesity may have increased in the Senegalese capital in five years (17%), but this difference was not statistically significant. However, since 2009, the prevalence of central obesity by WC has increased significantly, by 23% ($p < 0.05$). In Tessekere, the prevalence of overweight and obesity were 13.3 and 2.8%, respectively. Despite the difficulty of making comparisons with other West African rural areas due to the lack

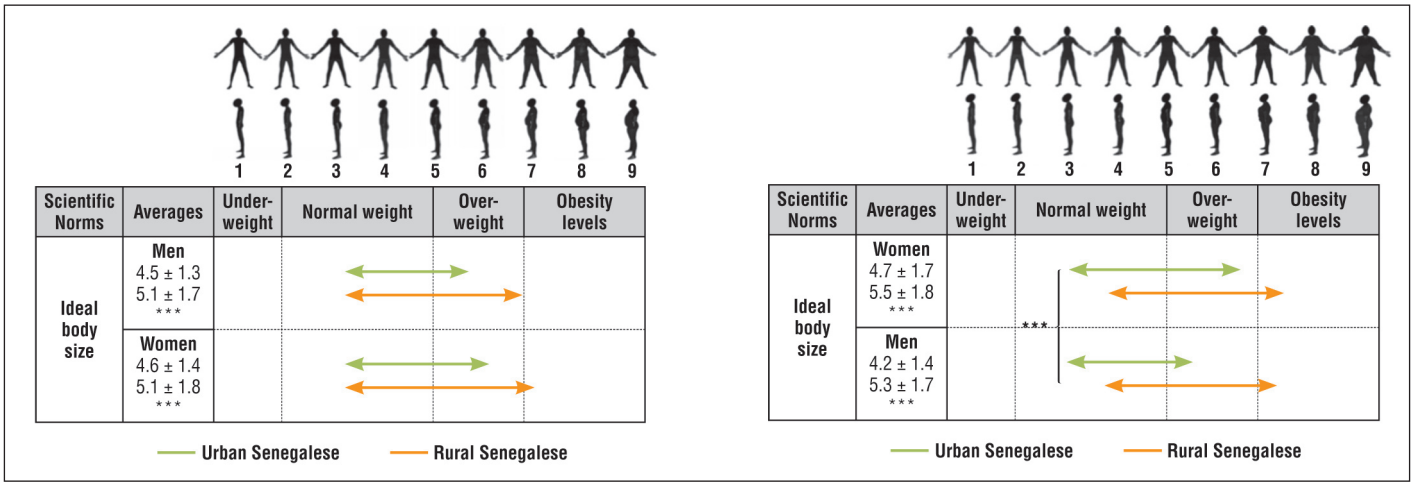

Figure 3. Perceptions of ideal body size on masculine and feminine body size scale.

of current data,[10] these results tend to indicate that Tessekere is also one of the rural areas in the sub-region that is least affected by the obesity epidemic.[33-35]

As indicated in the literature on West Africa,[10] problems of excess weight affect the urban environment more than the rural environment, therefore showing just how environmentally dependent the nutritional transition is in Senegal. In Dakar, the modern lifestyle[36] is combined with a decrease in physical activity and a higher calorie content diet. In Tessekere, where there is no running water or electricity, a pastoral lifestyle still protects the population from the obesity epidemic, particularly by obliging people to travel long distances daily to feed and water their herds.

However, our results show that such differences between the urban and rural environment may not last, as overweight and obesity rates among women born after the great drought of 1973–1974, *hitande bonde* [the worst year in Pulaar], are now approaching those of their urban counterparts. The gradual closing of the gap between urban and rural populations is also borne out by results concerning the ideal body size. In the rural environment, the ideal body type for both men and women is in the overweight category, whereas it is in the normal range in Dakar. The social value placed on the overweight body undeniably acts as a factor in the development of excess weight in rural areas.[16]

At the same time, it is important to note the considerable tolerance that both rural and urban Senegalese show toward overweight. At a BMI of 27.5 kg/m², less than 40% of the men in Dakar and Tessekere saw themselves as too fat, compared to 50% of urban women and 30% of rural women. By comparison, in France, for the same BMI, 60% of the men and 85% of women saw themselves as too fat.[29] Therefore, not only are body weight norms higher in Senegal than in France, but they are also less strict, which can only foster development of the obesity epidemic.[16] A tightening of these body weight norms is conceivable in the years to come, both pro-actively, through public health messages issued by the Senegalese government, and also through globalisation and the media, which convey beauty standards that emphasise a slimmer body, particularly in the urban environment.[37,38]

Our investigation has several limitations. First, the study design was cross-sectional, which does not allow us to explore causation. To overcome this limitation, it would be necessary to conduct a longitudinal study in Dakar in the future. Second, due to insufficient numbers of older adults in the study, we were unable to survey the evolution of body weight after 50 years of age, which should be analysed in the future, given the significant rise in weight-related problems with age, and the aging population on the continent.[39]

Conclusion

This study shows that the prevalence of obesity is bound to rise quickly among Senegalese women living in a rural environment, partly due to high body weight norms and a large tolerance towards overweight and obesity. To combat problems of obesity in Senegal at present, public health messages should be geared towards the population category most at risk, in other words mature women living in urban areas. However, to limit the scope of the epidemic over the entire country, health centres, which are the only local health structures in rural areas, must begin to raise awareness of the problems that arise with excess body weight.

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Any physical activity in elderly better than none at all for reducing cardiovascular risk

Any physical activity in the elderly is better than none at all for reducing cardiovascular risk, according to an 18-year study in more than 24 000 adults published recently in the *European Journal of Preventive Cardiology*. 'We know that regular physical activity has major health benefits,' said first author Dr Sangeeta Lachman, a cardiologist at the Academic Medical Centre, Amsterdam, the Netherlands.

'Healthy adults are advised to do at least 150 minutes a week of moderate intensity or 75 minutes a week of vigorous intensity aerobic exercise to reduce their risk of cardiovascular disease,' she continued. 'These recommendations are based primarily on research in middle-aged adults and we wanted to know whether regular physical activity yields comparable cardiovascular health benefits in elderly people.'

This study compared the association between different levels of physical activity and the risk of cardiovascular disease in middle-aged to elderly individuals. The hypothesis was that exercise would be equally beneficial in reducing cardiovascular risk in middle-aged and elderly individuals.

The study included 24 502 adults aged 39 to 79 years who participated in the European Prospective Investigation into Cancer (EPIC) Norfolk cohort, a prospective population study that is part of the ten-country collaboration EPIC study. The cohort was primarily designed to assess dietary and other determinants of cancer, but data were also collected on determinants of cardiovascular disease.

Participants were recruited between 1993 and 1997 from registries of general practices in the county of Norfolk, UK. On enrolment into the study, participants completed a health and lifestyle questionnaire, underwent a standardised physical examination and gave blood samples. Physical activity during work and leisure time was assessed with a questionnaire and participants were categorised as active, moderately active, moderately inactive and inactive.

Patients were followed up until 31 March 2015 for hospitalisation or death from cardiovascular events (coronary heart disease or stroke), which were identified by linking the participant's unique National Health Service number with the East Norfolk Health Authority (ENCORE) database.

Physical activity levels and time to cardiovascular events were investigated in three age categories: less than 55, 55 to 65 (middle-aged), and over 65 years of age (elderly).

During a median follow-up of 18 years there were 5 240 cardiovascular disease events. In elderly participants, hazard ratios for cardiovascular events were 0.86, 0.87 and 0.88 in moderately inactive, moderately active and active people, respectively, compared to inactive people. In those aged 55–65 and less than 55 years, the associations were directionally similar, but not statistically significant.

Dr Lachman said: 'We observed an inverse association between physical activity and the risk of cardiovascular disease in both middle-aged and elderly people. As expected, there were more cardiovascular events in elderly participants, which could explain why the association only reached significance in this age category.'

'Elderly people who were moderately inactive had a 14% reduced risk of cardiovascular events compared to those who were completely inactive,' continued Dr Lachman. 'This suggests that even modest levels of physical activity are beneficial to heart health. Elderly people should be encouraged to at least do low-intensity physical activities such as walking, gardening, and housework.'

She concluded: 'Given our aging population and the impact of cardiovascular disease on society, a broader array of public health programmes is needed to help elderly people engage in any physical activity of any level and avoid being completely sedentary.'

Drug Trends in Diabetes

Diabetes and cancer: is there a link?

An estimated up to 4.6 million people are living with diabetes in South Africa and an alarming 60 000 new cases of cancer are reported annually, according to the South African National Cancer Registry. Dr Jay Narainsamy, specialist physician/endocrinologist, Centre for Diabetes and Endocrinology (CDE), says, 'It is important to delve into the link between these two prevalent conditions in the hope that this understanding may lead to better lifestyle choices and positive changes in clinical management.'

The link between diabetes and cancer was considered as early as 1959. A report in the *New England Journal of Medicine* in March 2011 looked at causes of death in patients with diabetes. 'The article estimated cancer-related deaths at seven per 1 000 person-years and four per 1 000 person-years among men and women, respectively. Diabetes was associated with an increase in cancer-related deaths involving the pancreas, ovaries, liver, colorectum, breasts, lungs and bladder,' explains Narainsamy.

Diabetes and cancer have a number of common risk factors, some of which are modifiable and some not. Non-modifiable risk factors include age, gender and ethnicity, with increased risk in older people, men and in the African-American population in the United States. Modifiable risk factors include obesity, diet, physical activity, smoking and alcohol abuse.

'Obesity is linked to the development of insulin resistance and type 2 diabetes. It is thought that the high levels of insulin produced by the body to compensate for insulin resistance and obesity-associated inflammation may precipitate cancer development,' says Narainsamy. 'In addition, diabetes itself (especially if not controlled) may cause vascular damage and an inflammatory state, which may create an environment for tumour development.'

Diets low in processed meats, red meats and with a high content of vegetables, fruit and whole grains aid in lowering the risk of developing certain cancers. A healthy diet may also lead to weight loss and reduce the risk of developing insulin resistance and diabetes. Increased physical activity has been shown to reduce the risk of certain types of cancer as well as improving overall health. Smoking and alcohol intake are both associated with the development of cancer as well as diabetes.

'On a further positive note, the oral diabetes medication, metformin, which is our first-line drug of choice for patients with type 2 diabetes, has been shown to inhibit abnormal cell growth and has potential anti-cancer properties. Further studies are currently underway to assess the interaction between metformin and cancer, she says.

The link between diabetes and cancer in the other classes of oral diabetes agents are, however, less conclusive. 'On the opposite spectrum, injectable insulin was thought to be associated with an increased risk of cancer development. However, this has not been conclusively proven and risk is probably better evaluated in the context of duration of diabetes, other oral diabetes agents already on board and poor glycaemic control.'

'There is undoubtedly a link between diabetes and the development of certain types of cancer. With this in mind, it is important that doctors ensure that routine screenings for at-risk patients are completed timeously. They also need to be vigilant for "red flag" complaints and act promptly to investigate these problems,' says Narainsamy. 'While further research still needs to be done on the links between diabetes and cancer, the positive take-away message is that foundational lifestyle therapies for diabetes, including healthy eating, increased physical activity, weight loss and not smoking, as well as our first-line pharmacological therapy, metformin, may have the additional benefit of reducing your cancer risk,' she concludes.

Placing diabetes management firmly on the table

'The diabetes tsunami is here. Unless we meet it head on with appropriate management, this condition is single-handedly set to break the healthcare system, if not the entire economy, in the next decade. This is the view of Dr Larry Distiller, specialist physician/endocrinologist and principal physician, and executive chairman of the Centre for Diabetes and Endocrinology (CDE).

Dr Larry Distiller

Distiller says at this time of year, when many schemes are announcing their benefits packages for 2018, and people with diabetes are mulling over their medical aid options, it is important to review what programmes are in place for the management of diabetes. He says that unfortunately, diabetes is often treated 'on the cheap' to save costs in the short term. 'A patient not seeing a nurse and registered dietitian costs less than someone who does. While no care may look cheaper than good care in the short term, we know that this is definitely not the case in the longer term. If we look at UK data, we see that complications of uncontrolled diabetes account for most of the overall costs of the condition (80%), while treatment and management only accounts for 8%.'

Distiller says it is regrettable that diabetes is often not 'treatable' due to the cost barriers for the patient. Just because you have medical aid does not guarantee that you will automatically receive care.

'When you consider diabetes remains the most common cause of blindness in the Western world, the leading cause of kidney failure, dialysis and transplantation and the most common factor in lower-limb amputations, this lack of care becomes significant,' he says. It is linked closely to the other well-known risk factors for heart disease and death, namely high blood pressure, high cholesterol levels and obesity and is also a major cause of acute hospitalisation.

'Good management of diabetes has the potential to reduce acute hospitalisation rates

for diabetes by 85%, eye complications and renal failure by 60% and amputation rates by over 80%. The potential cost savings run into billions of Rands,' he says.

Distiller says the problem is that diabetes, despite its prevalence, is both an expensive and difficult condition to treat. 'It requires ongoing, in-depth management, education, monitoring and constant review and intensification of medication, with many patients eventually requiring insulin for control. And, as complications develop, the cost of management goes up incrementally and exponentially. As we know, diabetes is linked closely to the other well-known risk factors for heart disease and death, namely high blood pressure, high cholesterol levels and obesity.'

Against the backdrop of increasingly scarce and costly healthcare resourcing, and escalating, but preventable, costs of admissions for diabetes and complications of poor diabetes care, it is imperative that the healthcare sector urgently seeks integrated approaches to preventative, community-based diabetes care.

'We are clearly lacking critical research funding and resources to improve healthcare and treatment and there is an urgent need for more education and a change in the way diabetes is managed and funded in South Africa,' Distiller says.

'The real challenge is finding a way of reducing costs without impacting on quality of care. We appreciate that medical schemes are under enormous pressure to manage their costs, but it is concerning when the focus moves to cost-saving rather than greater patient service utilisation and improved clinical outcomes. We need to start being far more pro-active in treating and promoting patient health, particularly when one considers economic studies from the US showing that in people with diabetes, in-patient hospital care accounts for 43% of the total medical costs of diabetes and that poor long-term clinical outcomes increase the cost burden of managing diabetes by up to 250%.'

Distiller shared that over the last 23 years, CDE diabetes management programmes have resulted in a significant overall reduction in all acute diabetes-related hospital admissions. 'We have seen a reduction as high as 40% in all-cause hospital admissions and a 20% reduction in the length of hospital stays. This can only be good for funders who choose to utilise our services.'

Distiller highlighted that one of the challenges in the past was that these programmes were largely confined to medical scheme members on the top-end options. 'We have been working hard to ensure that CDE programmes of care can now be customised to ensure that scheme members on lower-benefit options are not excluded and that education platforms are extended.'

'The bottom line is that the most important person in the management of diabetes is the person living with diabetes. The majority of diabetes care is self-administered. The best results are without doubt where there is co-ordinated and continuous support for patients by a team of properly skilled doctors and allied health professionals in a defined programme of care, concludes Distiller.

Can diabetes be cured?

Being diagnosed with diabetes is often overwhelming for a person. Living with it can be just as hard.

Hamish van Wyk

Hamish van Wyk, registered dietitian and diabetes educator from the Centre for Diabetes and Endocrinology (CDE), says there is so much misinformation regarding how best to live with, or even 'cure', diabetes. Van Wyk says before addressing that point it is important to unpack the difference between type 1 diabetes and type 2 diabetes.

Type 1 diabetes affects around five to 10% of people with diabetes and is an auto-immune condition whereby the body attacks the insulin-producing beta-cells of the pancreas. This results in people needing insulin from the day of diagnosis to ensure healthy blood glucose levels. At this stage, it unfortunately cannot be cured.

Type 2 diabetes, on the other hand, affects the biggest group of people, approximately 90 to 95% of those with diabetes. It is largely associated with lifestyle factors including urbanisation, westernisation, nactivity, being overweight, and unhealthy patterns of nutrition, which express an underlying genetic predisposition.

Van Wyk says that fat distribution is particularly important; too much fat around the waistline (central, visceral or abdominal obesity) is both the initial cause and the continuing driver of an ongoing vicious circle of dysfunctional metabolic processes. These result in declining production of the blood glucose-lowering hormone insulin, resistance to the effects of insulin and deposition of excess toxic fat in the liver and pancreas. This situation leads to an increasing need for therapies to manage diabetes, including eventually, insulin therapy.

The big question is, can type 2 diabetes actually be cured? 'The simple answer is no,' says van Wyk. 'The damaged cells in one's pancreas will always be damaged. One can however reduce or even cure insulin resistance and you can place type 2 diabetes into remission.'

'As with cancer, type 2 diabetes can be placed into remission; medication will no longer be required and the person's blood glucose levels will remain normal.'

Van Wyk says, 'Despite remission being possible, it is often not achieved through conventional moderate calorie-restricted diets, where only 11.7% of people go into remission. However, through very low-calorie diets (< 800 kcal a day) we see a very different picture; remission can be achieved within one week! It appears that the key is the very low-calorie content of the diet.'

The latest published data from 2016 shows that after eight weeks on a very low-calorie diet, up to 87% of people who had diabetes for less than four years went into remission. 'The length of time one has had diabetes is very important and unfortunately, this fact is not coming across in consumer articles. If you have had diabetes for 10 years or more, you are less likely to go into remission even if you follow a strict nutritional regimen. Around 50% of these patients achieve remission,' he says.

Nevertheless, even if one can't go into remission, the research shows that by following a very low-calorie diet and using the 'break' to re-establish a new and healthier relationship with food, you can still benefit from huge reductions in insulin and/or oral medication while improving your weight and blood glucose levels.

To find out more about how to place diabetes in remission, find the following link www.cdediabetes.co.za

Diabetes News

Innovation needed to provide all citizens of South Africa with essential healthcare

A great deal has been documented about the challenges that South Africa faces in the provision of adequate primary healthcare, with the cost of healthcare acting as one of the foremost barriers to access across the continent. Other factors include a lack of qualified healthcare workers, and a shortage of electricity, water and basic technology.

In early October this year, the white paper for the much debated National Health Insurance (NHI) system was released for public comment. With only 20% of South Africans making use of private healthcare due to exorbitant prices, the public healthcare system has been under immense pressure to serve the majority of the population.

Healthcare in South Africa is a study in contrasts, which requires a two-pronged approach, addressing both ends of the healthcare spectrum; catering for the needs of people who currently don't have access to even basic quality primary healthcare on the one hand, and addressing the rising incidence of non-communicable diseases on the other.

The NHI emphasises a new way of thinking in health governance that is needed to reshape the health of South Africa. 'There are a number of significant areas where our healthcare system must transform if we are going to succeed in delivering long-term, value-based care," says Jasper Westerink, chief executive officer, Philips Africa.

Governments cannot be expected to tackle or change the challenges facing the healthcare continuum alone. It has become more important than ever for them to partner and enable businesses and NGOs to work collectively in public–private partnerships. A more connected and integrated form of healthcare is key to better serve future generations.

Philips, a global leader in health technology, emphasises the importance of advancing primary healthcare by creating sustainable improvement to address a wide range of challenges collectively. To address these issues, the company is creating solutions that connect people, technology and data seamlessly across the care continuum, which they showcased in Johannesburg at their Philips Live! Innovation Experience.

The technologies and platforms that Philips is introducing locally are increasing the efficiency of healthcare for both care provider and patients and are intended to reshape the health of the nation.

The Philips Live! Innovation Experience showcased technological innovations that deliver ever-greater precision and minimally invasive interventions, allowing clinicians to accurately diagnose and provide the best treatment the first time round, for some of the most challenging cardiovascular conditions and procedures. The experience also demonstrated locally relevant technologies and solutions to help address the complicated and multifaceted problems facing primary healthcare in South Africa.

In a landscape with escalating costs, changing regulations and fewer medical resources, innovations, on-going awareness campaigns and conversations all highlight the progress that is being made in the journey to provide the right care at the right time to all patients.

'I look forward to being on the frontline as we continue to bring technology, data and people together and as we come up with even more innovative solutions that can make people's lives better in a real and measurable way,' concludes Westerink.

Prediabetes intervention cuts cardiovascular risk

According to research presented at the annual meeting of the American Diabetes Association (scientific session of 16 June 2014), treatment of prediabetes and restoration of normal glucose regulation (NGR) reduces cardiovascular risk.

Dr Leigh Perreault of the University of Colorado Denver School of Medicine in Aurora and colleagues analysed cardiovascular risk for 2 775 participants in the Diabetes Prevention Program Outcomes Study, who were randomly assigned to intensive lifestyle modification, metformin, or placebo. Cardiovascular risk was assessed by Framingham score and individual risk factors for cardiovascular disease.

The researchers found that Framingham scores according to glycaemic exposure did not differ between the groups. During 10 years of follow up, mean Framingham scores were highest among those in the prediabetes group (16.2 versus 15.2 in those restored to NGR and 14.3 in those with diabetes), but this score declined over time. Higher medication use for treatment of elevated lipid and blood pressure levels partly explained the lower Framingham score in the diabetes group versus the other groups, a declining Framingham score in the pre-diabetes group, and favourable changes in individual cardiovascular risk factors.

Regardless of type of initial treatment, participants who did not develop diabetes had a 28% lower occurrence of the microvascular complications than those participants who did develop diabetes, a co-author said in a statement. 'These findings show that intervening in the prediabetes phase is important in reducing early-stage complications.'

Source:

http://www.diabetesincontrol.com/articles/53-/16479-ada-prediabetes-intervention-cuts-cardiovascular-risk

Rooibos could reduce risk of 'type 3' diabetes: a precursor to Alzheimer's disease

Researchers at Warren Alpert Medical School at Brown University in the US found a link between a relatively new form of diabetes, known as 'type 3' diabetes and Alzheimer's disease.

As with all types of dementia, Alzheimer's is caused by a combination of genetic, lifestyle and environmental factors that affect the health of the brain over a period of time, but now scientists have discovered a strong connection between the disease and insulin resistance in the brain; also referred to as type 3 diabetes.

Prof Christo Muller, chief specialist scientist at the SA Medical Research Council (SAMRC) describes Alzheimer's as a neurodegenerative disease in the aged, which involves the progressive loss of nerve cells and connections. 'Type 1 and 2 diabetes are typically characterised by hyperglycaemia (high blood sugar) whereas type 3 diabetes is a more complex disease that has its origin in the central nervous system.

'Many type 2 diabetes patients have deposits of a protein called beta-amyloid in their pancreas, which is similar to the protein deposits found in the brain tissue of Alzheimer's sufferers. According to research published in the World Journal of Diabetes, this increases type 2 diabetes patients' risk of Alzheimer's disease by between 50 and 65%," remarks Muller.

Current research suggests that rooibos has the potential to delay or prevent the onset and progression of type 2 diabetes, however its effect on the associated risk of type 3 diabetes and Alzheimer's disease still needs to be elucidated.

Muller says phenolic compounds present in rooibos enhances the body's antioxidant defences, helping to fight a variety of oxidative stress-induced conditions. 'The brain is one of the organs most sensitive to oxidative stress, and long-term exposure to increased levels of free radicals causes damage to neural cells. Dietary anti-oxidants, such as those found in rooibos, could therefore protect vulnerable neurons against the impact of oxidative by-products.

'Rooibos tea is a rich source of dietary anti-oxidants, including flavonoids, such as dihydrochalcone glucoside, aspalathin and nothofagin. Aspalathin, in particular, helps to modify hormones in the body and reduces the output of adrenal hormones specifically, thus reducing stress and helping to inhibit metabolic disorders.

'Aspalathin also helps to regulate blood sugar and therefore can play a role in reducing the risk of type 2 diabetes and excessive fat production. Our research at the SAMRC found that an aspalathin-enriched extract of green rooibos was particularly effective at lowering raised blood glucose levels in diabetic rats. Aspalathin is a unique phenolic compound (a chemical produced by the plant to help protect itself from negative environmental factors) limited to the genus Aspalathus, which has demonstrated a significant contribution to the biological benefits of rooibos,' he says.

Studies conducted on the anti-diabetic properties of rooibos by the SAMRC and the Agricultural Research Council (ARC), including those done in overseas laboratories, span more than 10 years of intensive work. In a more recent study conducted by Prof Muller and his team of researchers from SAMRC, rooibos extract achieved significant glucose- and cholesterol-lowering results in diabetic primates, which has been described as a breakthrough discovery. Human trials have been earmarked for 2018.

'Rooibos, in conjunction with a healthy lifestyle is certain to benefit everyone,' concludes Prof Muller.

Currently, an estimated one in 14 South Africans between the ages of 21 and 79 years suffers from diabetes. Alzheimer's is reported to affect 750 000 South Africans.

For more info about how rooibos can benefit you, visit www.sarooibos.co.za

ECG rhythms CPD

CPD developed by Prof Rob Scott Millar, Cardiac Clinic, UCT/Groote Schuur Hospital

CPD overview: Following the introductory "Approach to Rhythms", this online educational CPD quiz will consist of a series of ECGs with a variety of important cardiac rhythms. Each will be accompanied by a series of questions, followed by a detailed analysis and explanation.

Target audience: Cardiologists, physicians, emergency unit doctors and anaesthetists. Including those studying for FCP and certificate in cardiology.

Total time commitment: ± 30 to 60 minutes.

Assessment information: A pass mark of 70% is required. A candidate has 60 days to complete the CPD after registration.

CPD certificate: A PDF certificate of completion will be issued on successful completion the CPD.

CPD enrollment fee: Free / no charge.

Important notice: The CPD was made possible by an unrestricted educational sponsorship from Bayer Pharmaceuticals South Africa, which had no control over the content.

Publisher information: This CPD is endorsed by the *Cardiovascular Journal of Africa* published by Clinics Cardive Publishing.

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Carzin XL. Each film coated tablet contains 4 mg doxazosin. Reg. No.: RSA S3 41/7.1/0557. NAM NS2 10/34/0376. For full prescribing information, refer to the package insert approved by the Medicines Control Council, July 2009.
1) Pompeo ACL, *et al.* A randomised, double blind study comparing the efficacy and tolerability of controlled release Doxazosin and tamsulosin in the treatment of benign prostatic hyperplasia. Int J. Clin Pract Oct 2006;60(10):1172-1177. **2)** Kirby RS, *et al.* A Combined analysis of double-blind trials of the efficacy and tolerability of doxazosin-gastrointestinal therapeutic system, doxazosin standard and placebo in patients with benign prostatic hyperplasia. British Journal of Urology International 2001 Feb;87(3):192-200. **3)** Carzin XL package insert. **4)** Vs. Doxazosin XL originator 4 mg modified release formulation. Department of Health website. *http://www.mpr.gov.za* - Accessed 21/05/2015.
CLXC73/01/2015