





ORIGINAL RESEARCH

Posture-Related Differences in Cardiovascular Function Between Young Men and Women: Study of Noninvasive Hemodynamics in Rural Malawi

Manoj Kumar Choudhary , MD, PhD*; Roosa-Maria Penninkangas, BM*; Arttu Eräranta , MSc, PhD; Onni Niemelä , MD, PhD; Charles Mangani , MBBS, PhD; Kenneth Maleta , MBBS, PhD; Per Ashorn , MD, PhD; Ulla Ashorn , PhD†; Ilkka Pörsti , MD, PhD†

BACKGROUND: Cardiovascular risk is higher in men than in women, but little information exists about sex-related differences in cardiovascular function from low-income countries. We compared hemodynamics between sexes in rural Malawi in a cohort followed up since their birth.

METHODS AND RESULTS: Supine, seated, and standing hemodynamics were recorded from 251 women and 168 men (mean age, 21 years; body mass index, 21 kg/m²) using oscillometric brachial waveform analyses (Mobil-O-Graph). The results were adjusted for estimated glomerular filtration rate, and plasma potassium, lipids, and glucose. Men had higher brachial and aortic systolic blood pressure and stroke index regardless of posture ($P<0.001$), and higher upright but similar supine diastolic blood pressure than women. Regardless of posture, heart rate was lower in men ($P<0.001$), whereas cardiac index did not differ between sexes. Women presented with lower supine and standing systemic vascular resistance index ($P<0.001$), whereas supine-to-standing increase in vascular resistance ($P=0.012$) and decrease in cardiac index ($P=0.010$) were higher in women. Supine left cardiac work index was similar in both sexes, whereas standing and seated left cardiac work index was higher in men than in women ($P<0.001$).

CONCLUSIONS: In young Malawian adults, men had higher systolic blood pressure, systemic vascular resistance, and upright cardiac workload, whereas women presented with higher posture-related changes in systemic vascular resistance and cardiac output. These findings show systematic sex-related differences in cardiovascular function in a cohort from a low-income country with high exposure to prenatal and postnatal malnutrition and infectious diseases.

Key Words: blood pressure ■ cardiovascular disease ■ hemodynamics ■ left cardiac work ■ pulse wave velocity ■ sex

Biological sex plays a significant role in the incidence and outcome of cardiovascular disease (CVD). Particularly, before middle age, men experience more cardiovascular events than women.^{1–4} In the FHS (Framingham Heart Study), the lifetime risk for CVD at the age 40 years was about 49% for men and 32% for women.² Lower CVD risk in women may

be largely explained by the protective influences of estrogens on the cardiovascular system.⁴ In addition to hormonal differences, the disparity in the CVD risk between sexes has been attributed to a more favorable risk factor profile, including lower plasma lipids, in women. However, the sex difference in the incidence of CVD diminishes with increasing age.^{3,5}

Correspondence to: Ilkka Pörsti, MD, PhD, Faculty of Medicine and Health Technology, FI-33014 Tampere University, Tampere, Finland. E-mail: ilkka.porsti@tuni.fi

*M.K. Choudhary and R.-M. Penningkangas are co-first authors.

†U. Ashorn and I. Pörsti are co-senior authors.

Supplemental Material for this article is available at <https://www.ahajournals.org/doi/suppl/10.1161/JAHA.121.022979>

For Sources of Funding and Disclosures, see page 9.

© 2022 The Authors. Published on behalf of the American Heart Association, Inc., by Wiley. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- Human beings spend their active life in the seated or standing position, but only few studies have compared upright regulation of the cardiovascular system between sexes, and no studies have examined subjects from low-income countries.
- Higher posture-related changes in cardiac output and systemic vascular resistance in women, and higher upright but not supine left cardiac work in men, correspond to previous findings by our research group.
- These differences were observed in a cohort exposed to prenatal and postnatal malnutrition, growth stunting, and severe infectious diseases, indicating that the above differences in upright hemodynamics between sexes were not related to ethnicity.

What Are the Clinical Implications?

- The posture-related variations in hemodynamics may play a role in the differences of cardiovascular risk between sexes.
- The present results showed higher systolic blood pressure (BP), and higher supine-to-standing increase in diastolic BP in men than in women, whereas both sexes presented with systematic posture-related changes especially in diastolic BP.
- These findings raise the question whether seated BP measurements alone are sufficient, and whether evaluation of the cardiovascular status should routinely include measurements of BP in the supine, seated, and standing postures.

Nonstandard Abbreviations and Acronyms

LCWI	left cardiac work index
PWV	pulse wave velocity
SVRI	systemic vascular resistance index

Several distinctive changes in cardiovascular regulation and structure have been reported between sexes. In young women, blood pressure (BP) and the incidence of hypertension are lower than in young men.⁶ A possible need for a lower definition of optimal systolic BP in women than in men was recently recognized.⁷ In early adulthood, pulse pressure is also lower in women than in men; however, at older ages, pulse pressure becomes gradually higher in women.⁸ Women have

smaller heart chamber size and left ventricular mass, lower ventricular ejection rate, and lower oxygen carrying capacity attributable to lower hemoglobin concentration than men.^{9,10} When examined using magnetic resonance imaging, women had a higher left ventricular ejection fraction but similar cardiac index compared with men.¹¹ Arterial stiffness, which can be evaluated by measuring aortic pulse wave velocity (PWV), is usually lower in women than in men.^{12,13}

Although a major portion of our active life is spent in the upright position, most studies on hemodynamics between sexes have focused on supine measurements.^{4,11,14} When body position changes from supine to upright, blood pools to the lower extremities, resulting in decreased stroke volume and cardiac output. As compensatory mechanisms, the sympathetic nervous system is activated with subsequent increases in heart rate and systemic vascular resistance to maintain the level of BP.^{15–17} However, individual differences exist, and upright hemodynamic regulation can be divided into different phenotypes according to the magnitude of the parallel changes in vascular resistance and cardiac output.¹⁸ Previously, supine and seated systolic BP was found to be lower in women than in men, but no differences in diastolic BP were observed.^{11,19} Recently, we found that the notable difference in cardiovascular function between sexes was lower upright left cardiac workload in women, a finding that was not explained by known cardiovascular risk factors or hormonal differences before menopause.^{20,21}

Only limited information exists comparing the upright regulation of the cardiovascular system between sexes, and none of the above studies has examined subjects from low-income countries with a high prevalence of malnutrition, infectious diseases, and growth stunting.^{22–25} In this study, we examined putative posture-related hemodynamic differences between 21-year-old Malawian men and women, who had been followed up since their birth.

METHODS

Participants

The data that support the findings of this study are available from the corresponding author on reasonable request. This prospective cohort study was conducted in Lungwena, Mangochi District, Southern Malawi. The study participants originally comprised 795 mothers who attended antenatal clinic at Lungwena health center during their pregnancies between June 1995 and August 1996. These women carried altogether 813 fetuses, and the number of children born alive was 767.²² From the original study cohort, 50 participants were lost to follow-up and 179 subjects were deceased by the age of 15 years.²⁶ When the subjects were aged

~21 years, they were invited to participate in noninvasive hemodynamic recordings. Altogether, 429 young adults agreed to participate, and successful BP recordings and measurements of weight and height were performed in 419 subjects. Details of recruitment, data collection with information about school education, and follow-up have been described previously.²² Length and height measurements were converted to Z-scores by using World Health Organization MGRS (Multicenter Growth Reference Study) for children data²⁷ and the 2007 World Health Organization reference curves (5–19 years).²⁸

The study complies with the Declaration of Helsinki, and ethical approval for the LCSS (Lungwena Child Survival Study) was obtained from the National Health Science Research Committee in Malawi (93/94) and the College of Medicine Research and Ethics Committee. Informed consent was obtained from each guardian in the beginning of the cohort study and again from each young adult at the age of 21 years. The present study population consisted of 251 women and 168 men, with the age range being 20.3 to 22.3 years in women and 20.3 to 22.2 years in men (Table).

Evaluation of Food Insecurity and Living Environment

Food Insecurity

A modification of the Household Food Insecurity Access Scale of the Food and Nutrition Technical Assistance III project by the US Agency for International Development was used with 9 key questions.²⁹ Each of the questions had 4 answering options: never, rarely, sometimes, and often, and these were scored 0, 1, 2, and 3, respectively (Data S1). The food insecurity score for each participant was calculated by summing up the scores for each frequency-of-occurrence question.

The *living environment* was characterized by 6 questions modified from population and housing census questionnaire, Republic of Malawi (Data S2).³⁰ As the number of the answer options to these questions varied, the mean value of all participant answers to each question was adjusted to 0 and the SD was adjusted to 1. The living environment total score for each participant was calculated by summing up the standardized values for each question.

Laboratory Analyses

Blood sampling was performed during the study visit. On site, blood hemoglobin concentration was determined from a droplet of blood (HemoCue, Angelholm, Sweden), and the presence of falciparum malaria was examined using SD Bioline Malaria Ag Pf test (Standard Diagnostic Inc, South Korea), which is a 1-step, rapid, qualitative test for the detection of histidine-rich protein II specific to *Plasmodium falciparum* in human

Table. Clinical and Laboratory Characteristics of the Study Population

Characteristic	Women (n=251)	Men (n=168)
Age, y	21.3 (0.4)	21.3 (0.4)
Height, cm	156.0 (5.7)	165.7 (6.2)*
Weight, kg	52.0 (7.3)	58.0 (6.5)*
Body mass index, kg/m ²	21.4 (2.4)	21.1 (1.9)
Mean height/length-age Z-score		
During the first 6 mo of life	-1.88 (1.09)	-1.96 (1.24)
At the age of 21 y	-1.29 (0.94)	-1.71 (0.90)*
Time at school, y	3.6 (2.9)	4.6 (3.6)*
Ability to read and write, n/%		
No, n/%	146/58	76/45*
With difficulties, n/%	42/17	28/17
Fluent, n/%	63/25	64/38*
Food insecurity sum score	9 (5)	9 (5)
Standardized living environment sum score	0.06 (3.16)	-0.17 (3.05)
<i>Plasmodium falciparum</i> : positive rapid test, n/%	43/17.1	30/17.9
eGFR, mL/min per 1.73 m ²	130 (12)	128 (10)*
Hemoglobin, g/L	134 (15)	156 (15)*
Sodium, mmol/L	138 (3)	139 (2)
Potassium, mmol/L	4.0 (0.4)	4.1 (0.4)*
CRP, mg/L	0.9 (0.5–2.2)	0.9 (0.4–1.7)
Creatinine, μmol/L	51.8 (8.8)	69.9 (10.5)*
Total cholesterol, mmol/L	3.3 (0.7)	3.0 (0.6)*
Triglycerides, mmol/L	0.7 (0.5–1.0)	0.8 (0.6–1.1)*
HDL cholesterol, mmol/L	1.1 (0.3)	0.9 (0.2)*
LDL cholesterol, mmol/L	1.8 (0.6)	1.7 (0.5)*
Glucose, mmol/L	4.8 (0.7)	5.1 (0.7)*

Results shown as mean (SD), median (25th–75th percentile), or number/percentage of participants in each category. CRP indicates C-reactive protein; eGFR, estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration creatinine-based formula); HDL, high-density lipoprotein; and LDL, low-density lipoprotein.

* $P < 0.05$ vs women.

blood (sensitivity, 99.7%; specificity, 99.5%). Plasma was separated and stored at -70°C until cold shipping to Finland. The laboratory determinations were performed in SFS-EN ISO/IEC 15189:2013–accredited centralized laboratory at the Medical Research Unit, Seinäjoki Central Hospital, Seinäjoki, Finland. Plasma sodium, potassium, glucose, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglyceride, CRP (C-reactive protein), and creatinine concentrations were determined using Cobas c702 or Cobas c702 ion-selective electrode photometric assay tests (F. Hoffmann-Laroché Ltd, Basel, Switzerland). Estimated glomerular filtration rate was calculated using the Chronic Kidney Disease Epidemiology Collaboration creatinine-based formula.³¹

Hemodynamic Measurements

The research team in Lungwena, which has 20 years of experience in child health–related research, performed the recordings. Values of brachial and aortic BP, heart rate, stroke volume, cardiac output, systemic vascular resistance, and waveform-derived evaluation of PWV were obtained using an automated oscillometric device (Mobil-O-Graph; I.E.M., Stolberg, Germany). The values were normalized to body surface area using the Mobil-O-Graph software and expressed as cardiac index, stroke index, and systemic vascular resistance index (SVRI). Left cardiac work index (LCWI) was calculated using the following formula: $0.01439 \times (\text{mean aortic pressure} - \text{pulmonary artery occlusion pressure}) \times \text{cardiac index}$.^{20,21,32} Pulmonary artery occlusion pressure was assumed to be 6 mm Hg (normal), 0.0143 is the conversion factor of pressure from millimeters of mercury to centimeters of water, volume to density of blood (in kg/L), and centimeters to meters. Cuffs were chosen according to the measured left upper arm circumference. The supine-to-upright change in the hemodynamic variables was calculated as the value in the standing posture minus the value in the supine posture.

The Mobil-O-Graph has been validated for measurement of peripheral and central BP^{33,34} and 24-hour ambulatory BP measurement, according to the British Hypertension Society³⁵ and European Hypertension Society criteria.³⁶ Also, the evaluated PWV has been compared with tonometric devices and invasively obtained values.³⁷

Experimental Protocol

Hemodynamics were recorded in the seated, supine, and standing postures using the Mobil-O-Graph in a quiet room. The BP cuff was attached, and after getting accustomed in the seated position for at least 5 minutes, the measurements using the Mobil-O-Graph device were taken twice. Then, the participants rested in supine position for 5 minutes and the third measurement was performed at the end of this period. The fourth and the fifth measurements were performed after about 5 minutes of standing. Thus, the protocol contained the supine-to-upright change in body position to comply with the approved approach to examine orthostatic BP responses.³⁸ For practical reasons, the protocol contained 5 successive BP recordings, as all measurement were to be performed within a specific time frame to ensure the compliance of the participants. In the figures, the results are presented in the order of supine, seated, and standing.

Statistical Analysis

The demographic and laboratory characteristics between women and men were analyzed using independent-samples *t*-test for normally distributed

variables and Mann-Whitney *U*-test for variables with skewed distribution. The homogeneity of variances was tested with the Levene test, and Pearson correlation coefficients were calculated, as appropriate.

Hemodynamic differences between sexes in the supine, seated, and standing positions were examined using generalized estimating equations. This method enabled the analyses of repeated measurements of hemodynamic variables to examine the influences of sex, posture, and their interaction on the variable of interest. Linear scale response was applied, and the autoregressive option was chosen for the correlation matrix, as successive serial measures of hemodynamics in individual participants are autocorrelated. As the participants presented with differences in estimated glomerular filtration rate, and plasma concentrations of potassium, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and glucose (Table), the analyses were adjusted for these differences by using the variables as covariates. The PWV analyses were additionally adjusted for mean aortic pressure according to the expert consensus.³⁹ The *t*-test was applied for the analyses of the supine-to-upright changes in the hemodynamic values.

Information about missing data is presented in Table S1. Missing data were observed at random, altogether 387 participants had complete data sets, whereas a maximum of 1 missing value was observed in 412 participants. The results were presented as mean and SD or as median and 25th to 75th percentile in the tables, and as mean and SEM in the figures, and $P < 0.05$ was considered statistically significant. SPSS version 26.0 (IBM SPSS Statistics, Armonk, NY) was used.

RESULTS

Study Population and Laboratory Values

The demographic and laboratory data of the 251 (60%) women and 168 (40%) men are presented in the Table. At the age of 21 years, male participants were taller and weighed more than the female participants. However, the mean length-for-age or height-for-age Z-score was similar in male and female participants during the first 6 months, but lower in men at the age of 21 years (Table).^{27,28} Because of the study design, the female and the male subjects had matching ages, and body mass index was also similar in both sexes. The number of years of school education was higher and the ability to read and write was more prevalent among men than women. The sum scores for food insecurity and the living environment, and the prevalence of positive rapid test for *P falciparum* did not differ between men and women (Table and Table S1). Estimated glomerular filtration rate was slightly higher, whereas blood hemoglobin and plasma concentrations of potassium,

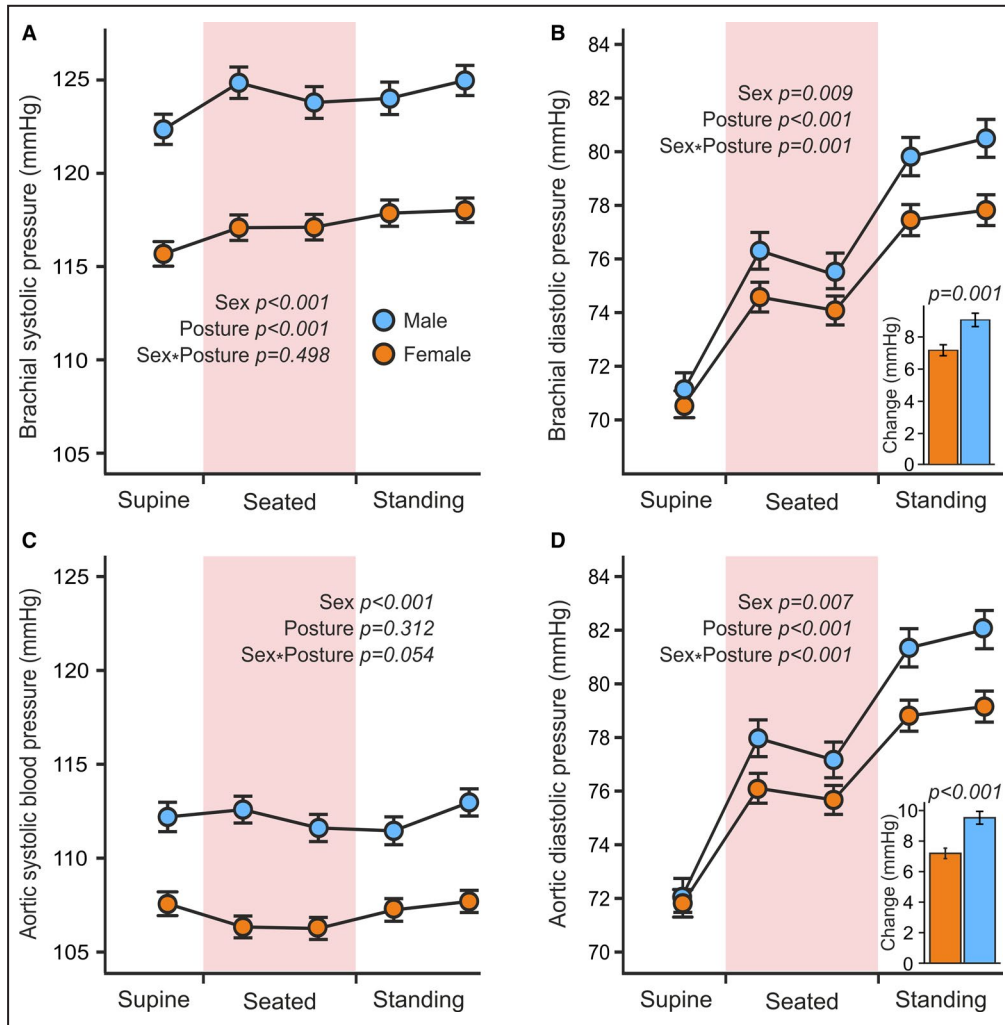


Figure 1. Line graphs show brachial systolic (A) and diastolic (B) and aortic systolic (C) and diastolic (D) blood pressure values in 251 women and 168 men during supine, seated, and standing positions.

B and D. Insets show the supine-to-upright increase in diastolic blood pressure; mean \pm SEM, statistics by generalized estimating equations (line graphs) with adjustments for estimated glomerular filtration rate, and plasma concentrations of potassium, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and glucose, and by *t*-test in the insets for changes in the variables.

creatinine, and glucose were lower in young women when compared with men. The lipid concentrations in plasma were low, but total cholesterol, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol were higher, whereas triglyceride concentration was lower, in women than in men (Table).

Noninvasive Hemodynamics

Regardless of posture, women had lower brachial and aortic systolic BP than men (Figure 1A and 1C). Supine brachial and aortic diastolic BP was similar in both sexes, but a significant interaction with posture was observed so that seated and standing diastolic BP remained at a lower level in women (Figure 1B and 1D). Both the brachial and aortic supine-to-standing

increases in diastolic BP were less marked in women than in men ($P \leq 0.001$) (insets in Figure 1B and 1D). In all measurements, brachial and aortic mean arterial BP was lower in young women than in men ($P = 0.036$ for supine mean aortic BP, and $P < 0.001$ for other measurements).

In the supine, seated, and standing positions, women had higher heart rate (Figure 2A) and lower stroke index (Figure 2B) than men. Women also presented with a higher supine-to-seated increase in heart rate (7.4 ± 0.4 versus 5.4 ± 0.5 beats/min; $P < 0.001$), whereas supine-to-standing increase in heart rate did not differ between sexes (18.6 ± 0.6 versus 17.0 ± 0.7 beats/min; $P = 0.077$). Supine-to-seated (-8.0 ± 0.6 versus -4.6 ± 0.8 mL/m²; $P = 0.001$), but not supine-to-standing (-13.6 ± 0.6 versus

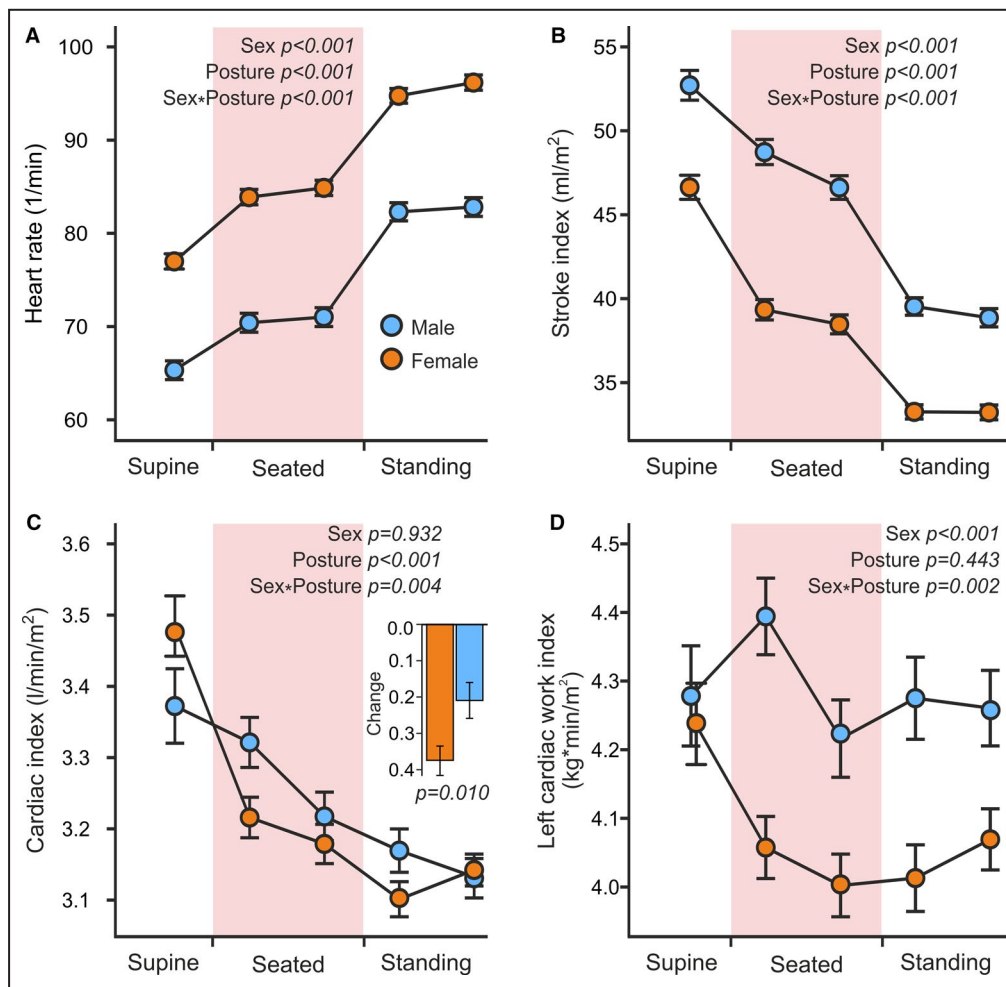


Figure 2. Heart rate (A), stroke index (B), cardiac index (C), and left cardiac work index (D) in male and female participants.

C, Inset shows the supine-to-upright decrease in cardiac index; statistics as in Figure 1.

-13.3 ± 0.8 mL/m²; $P = 0.789$), decrease in stroke index was more pronounced in women. However, cardiac index did not differ between sexes in the 3 postures (Figure 2C). Yet, a significant interaction with posture was observed, and women presented with a more pronounced supine-to-standing decrease in cardiac index ($P = 0.010$) (inset in Figure 2C). Supine LCWI was similar between sexes; however, seated and standing LCWI was lower in women than in men ($P < 0.001$) and a significant interaction with posture was present (Figure 2D). Accordingly, the supine-to-upright decrease in LCWI was more pronounced in women than in men (-0.22 ± 0.05 versus -0.01 ± 0.07 kg*min/m²; $P = 0.009$).

Young women presented with lower SVRI than men in the supine and standing positions, but not in the seated position (Figure 3A). A significant posture interaction was observed, and the supine-to-upright increase in SVRI was higher in women than in men ($P = 0.012$) (inset in Figure 3A). Regardless of posture,

young women had lower evaluated PWV than men (Figure 3B). However, the Pearson correlations between the supine, seated, and standing PWV values and the respective systolic BP levels were 0.889, 0.970, and 0.973. If height was included as a covariate in the analyses, all differences in the hemodynamic variables between women and men remained essentially the same. Furthermore, all above differences in hemodynamics between women and men were also present if estimated glomerular filtration rate and the plasma concentrations of potassium, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and glucose were not included in the analyses as covariates.

DISCUSSION

Our findings among a unique and well-characterized population of young adults from rural areas in Malawi demonstrate distinct sex-dependent characteristics in

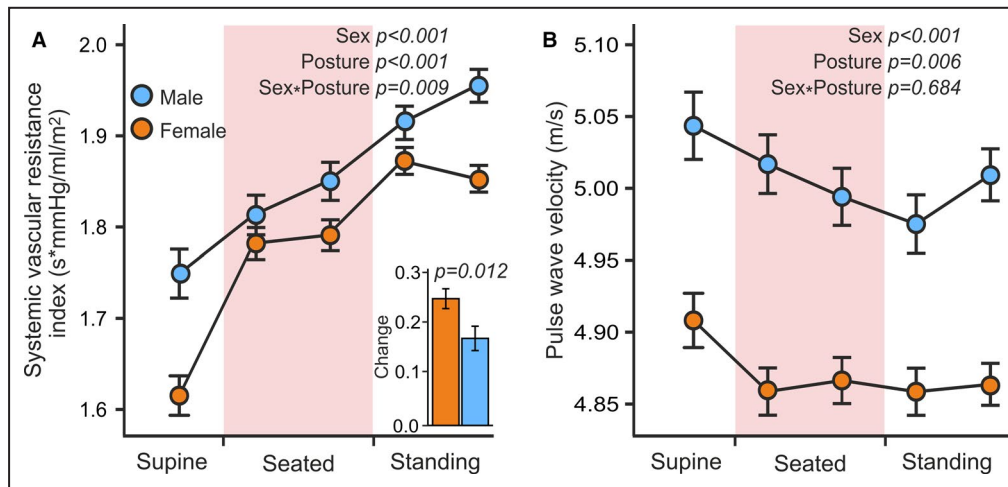


Figure 3. Systemic vascular resistance index (A) and waveform-derived evaluation of pulse wave velocity (B) in male and female participants.

A, Inset shows the supine-to-upright increase in systemic vascular resistance index; statistics otherwise as in Figure 1 but pulse wave velocity was additionally adjusted for mean aortic pressure.³⁹

cardiovascular function. In women, systolic BP, cardiac stroke volume index, supine and standing systemic vascular resistance, and large arterial stiffness (PWV) were all lower than those in men. Diastolic BP was also lower in the seated and upright positions in women, whereas supine diastolic BP was similar between sexes. The calculated left cardiac work was lower in young women in the seated and upright positions, but despite the higher systolic and mean BP in men, supine left cardiac workload was similar between sexes.

Androgens and estrogens may play an important role in the deviations of BP regulation between men and women,^{4,6,40} but the mechanisms of the sex-related differences in cardiovascular control are still poorly understood. In age group of 25 to 49 years, systolic BP is characteristically lower in women than in men, whereas in older age groups BP differences gradually recede and pulse pressure may even become higher in women.^{3,8} Although several studies have reported sex-related differences in cardiovascular function at rest,^{4–6,8,11,12,19} only few studies have compared upright BP and hemodynamics between sexes.^{17,20,21} Previously, lower supine and seated systolic BP was reported in women than in men, in the absence of differences in diastolic BP.^{11,19}

Central BP has been suggested to be a better predictor of cardiovascular risk than brachial BP,^{41,42} and in the present study both central and peripheral systolic BPs were higher in young men regardless of posture. Men also presented with higher aortic and brachial diastolic BPs in the standing position. However, although the supine-to-standing increases in diastolic BP were more pronounced in men, the supine brachial and aortic diastolic BPs were similar between sexes. Previously, higher supine-to-upright increase in

diastolic BP has been related with the risk of myocardial infarction in 1359 normotensive men during ~8.7 years of follow-up.⁴³ Moreover, in subjects with ≥ 10 mm Hg supine-to-standing increase in diastolic BP, the level of seated diastolic BP was also associated with the risk of myocardial infarction.⁴³ The more unfavorable upright hemodynamic load of the heart may predispose to earlier clinical manifestation of coronary heart disease in men.⁴⁴ Differences in the upright hemodynamic load on the heart may explain some of the differences in cardiovascular risk between men and women. The present results suggest that women could be more protected from cardiovascular events because of lower supine-to-standing increase in diastolic BP.

Previously, women with vasovagal syncope have presented with higher supine-to-standing BP variability.⁴⁵ Although postural orthostatic tachycardia appears to be more common in women than in men,⁴⁶ many reports indicate that men are actually more prone to vasovagal syncope than women.^{47,48} The measurement of BP variability could provide additional insight into the differences in hemodynamic and autonomic control between men and women.^{49,50} However, the present methods are not well suited to the study of BP variability, as only 1 supine and 2 seated and 2 standing BP values were recorded, which is a limitation of our study.

When evaluated by means of thoracic bioimpedance, 25 women presented with higher supine-to-standing increases in peripheral vascular resistance than 22 men,⁵¹ a finding corresponding well to the present results showing higher supine-to-upright increase in SVRI in women. During orthostatic stress, a lower increase in BP and muscle sympathetic nerve activity was reported in 8 women versus 9 men,⁵² and lower upright heart rate variability attributable to higher

sympathetic activity was found in 12 men versus 12 women.¹⁷ Accordingly, our previous results using analyses of heart rate variability indicated that women had lower cardiac sympathovagal balance as well as lower left ventricular workload, especially in the upright position, when compared with men.²⁰ Moreover, systematic differences in upright hemodynamics between sexes were not confined to premenopausal women, but were also observed in postmenopausal subjects, indicating that the variations between women and men were not solely explained by differences in sex hormones before menopause.²⁰ In the present study, we observed significant interactions between sex and posture for changes in diastolic BP but not for systolic BP. This was probably related to the higher posture-related increase in diastolic BP than in systolic BP in the participants. SVRI is more related to the level of diastolic BP than systolic BP, whereas large arterial stiffness is a more pronounced determinant of systolic BP.^{15,39} Significant interactions between sex and posture were also observed for heart rate, stroke index, SVRI, and LCWI, supporting the view of differences in the upright autonomic control of cardiovascular function between men and women.^{17,20,51,52}

Most of the sex-related studies on hemodynamics have been performed in middle- and high-income populations,^{13,20,21,51} and only little information is available from low-income countries. The present findings of higher posture-related changes in cardiac output and systemic vascular resistance in women, and higher upright but not supine left cardiac work in men, correspond well to our previous findings in 334 middle-aged normotensive subjects in Finland.²⁰ These findings are noteworthy because of the marked differences between the Finnish and the Malawian populations. Low socioeconomic status, maternal malnutrition, and child growth stunting attributable to deficient nutrition and infections are major issues in the low-income countries.^{22,23,25} Maternal malaria infection and low energy intake during pregnancy predispose the fetus to intrauterine growth retardation,^{23,53} whereas high incidence of preterm deliveries (22%) has been reported in Lungwena.⁵⁴ When compared with a high-income reference population, newborn babies in Malawi were ~2.5 cm shorter with ~500 g lower body weight.²⁴ During the first 6 months of age, high incidence of growth stunting (~70%) and low Z-scores of linear growth were observed in the present study population.²³ Moreover, the seroprevalence of HIV infection was high (18%) among the pregnant mothers of the present population.⁵⁴ Babies born to HIV-positive women are prone to faltering of weight gain and linear growth during infancy,^{24,53–56} and they do not express proper postnatal catch-up growth.⁵⁷ Subsequently, by the age of 15 years, 179 subjects of the present cohort had been deceased,²⁶ and the Z-scores of body height were lower than in the World

Health Organization reference populations^{27,28} at the participant age of 21 years (Table). Low-income and socioeconomic status, malnutrition, inflammation, and infections are all factors that can potentially influence the function of the cardiovascular system.^{58–60} In the present study, there were no differences in the scores for food insecurity and living environment between men and women. Moreover, 17% to 18% of the men and women tested positive for falciparum malaria that is endemic in Malawi.⁶¹ The Mangochi area has a high malaria transmission because of high temperature and frequent rainfall from October to April.⁶¹

Increased PWV is a strong acknowledged predictor of CVD and mortality, independent of the level of BP.⁶² In the present study, young men presented with higher waveform-derived PWV than women. However, the evaluated PWV values showed high correlations with systolic BP levels, and the results must be interpreted with caution. Indeed, Schwartz et al. reported that PWV evaluated by the Mobil-O-Graph was almost completely explained by age and systolic BP, and its relationship with carotid-femoral PWV was explained by the shared associations of arterial stiffness with age and systolic BP.⁶³ Nevertheless, sex is an acknowledged predictor of arterial stiffening, and men characteristically present with higher PWV than women.^{12,13,19} The present evaluated PWV values were within the normal limits reported for a large European population.⁶⁴ Magalhães et al. found that the PWV values in a healthy African population were consistent with the values of a normal European population aged <39 years.¹⁹ Ethnic differences in arterial stiffening may become apparent in older populations with prevalent cardiovascular risk factors.¹⁹

Previously, the hemodynamic features of Black and White Americans have been compared. Systemic vascular resistance was a significant predictor of ambulatory BP variation only in Black Americans but not in White Americans (n=10 in each group).⁶⁵ In response to 5 different stressor tests, 78 Black American men had higher systemic vascular resistance than 82 White American men, whereas the latter presented with greater changes in heart rate and cardiac output.⁶⁶ On the basis of impedance cardiography derived analyses of systemic vascular resistance and cardiac ejection, 76 Black American and 60 White American adolescents exhibited comparable myocardial and vasodilatory responses to heat stress, but Black Americans exhibited heightened myocardial and vasoconstrictive reactivity to cold stress.⁶⁷ In 5727 elderly subjects of the ARIC (Atherosclerosis Risk in Community) study, Black Americans displayed higher sensitivity to afterload-induced adverse changes in left ventricular structure and function than White Americans.⁶⁸ In the MESA (Multi-Ethnic Study of Atherosclerosis), Black Americans had lower small artery elasticity than White

Americans, indicating earlier vascular disease in the population of African ancestry.⁶⁹

In the present study, cardiovascular function was examined by the use of an oscillometric device validated for the measurement of peripheral and central BP.^{33,35} Many articles have also successfully compared the evaluated PWV values with tonometrically and invasively obtained values,^{33,35,37} but criticism concerning the PWV analysis has also been presented.⁶³ We have no reason to believe that the recordings would be less reliable in the upright position when comparing hemodynamics between sexes. Although cardiac output measurements in 24 hospitalized patients using Mobil-O-Graph gave slightly lower values than the invasive thermodilution method, the values were reproducible and the accuracy of the device was considered acceptable.⁷⁰ Cardiac output using Mobil-O-Graph also corresponded well to values measured using 2-dimensional transthoracic echocardiography.⁷¹

CONCLUSIONS

We found clear differences in upright hemodynamics between young women versus men in rural Malawi. Men presented with higher systolic BP and systemic vascular resistance than women. In men, upright position was associated with higher workload of the heart, whereas in the supine position cardiac workload was similar for both sexes. The female subjects presented with higher posture-related changes in systemic vascular resistance and cardiac output than male subjects. Corresponding findings were previously reported in a middle-aged Finnish population with different social and nutritional backgrounds and lower exposure to infectious diseases.²⁰ The present findings highlight systematic differences in the regulation of upright hemodynamics between women and men that are not related to the ethnic background.

ARTICLE INFORMATION

Received June 28, 2021; accepted December 31, 2021.

Affiliations

Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland (M.K.C., R.P., A.E., O.N., P.A., U.A., I.P.); Department of Laboratory Medicine and Medical Research Unit, Seinäjoki Central Hospital, Seinäjoki, Finland (O.N.); School of Public Health and Family Medicine, College of Medicine, University of Malawi, Blantyre, Malawi (C.M., K.M.); and Department of Pediatrics (P.A.) and Department of Internal Medicine (I.P.), Tampere University Hospital, Tampere, Finland.

Acknowledgments

The authors are deeply grateful to the study participants, the Lungwena team for data collection, and Paula Erkkilä, research nurse, for invaluable technical assistance in setting up the recording system on location in Lungwena, Malawi.

Sources of Funding

This work was financially supported by Nutriset S.A.S., Malaunay, France, Competitive State Research Financing of the Expert Responsibility Area

of Tampere University Hospital, Finnish Foundation for Cardiovascular Research, Sigrid Jusélius Foundation, and Pirkanmaa Regional Fund of the Finnish Cultural Foundation.

Disclosures

None.

Supplemental Material

Data S1–S2

Table S1

REFERENCES

- Kannel WB, Wilson PWF. Risk factors that attenuate the female coronary disease advantage. *Arch Intern Med*. 1995;155:57–61. doi: 10.1001/archinte.1995.00430010063008
- Lloyd-Jones DM, Larson MG, Beiser A, Levy D. Lifetime risk of developing coronary heart disease. *Lancet*. 1999;353:89–92. doi: 10.1016/S0140-6736(98)10279-9
- Jousilahti P, Vartiainen E, Tuomilehto J, Puska P. Sex, age, cardiovascular risk factors, and coronary heart disease. *Circulation*. 1999;99:1165–1172. doi: 10.1161/01.CIR.99.9.1165
- Hart EC, Joyner MJ, Wallin BG, Charkoudian N. Sex, ageing and resting blood pressure: gaining insights from the integrated balance of neural and haemodynamic factors. *J Physiol*. 2012;590:2069–2079. doi: 10.1113/jphysiol.2011.224642
- Russo G, Pintaudi B, Giorda C, Lucisano G, Nicolucci A, Cristofaro MR, Suraci C, Mulas MF, Napoli A, Rossi MC, et al. Age- and gender-related differences in LDL-cholesterol management in outpatients with type 2 diabetes mellitus. *Int J Endocrinol*. 2015;2015:e957105. doi: 10.1155/2015/957105
- Reckelhoff JF. Gender differences in the regulation of blood pressure. *Hypertension*. 2001;37:1199–1208. doi: 10.1161/01.HYP.37.5.1199
- Ji H, Niiranen TJ, Rader F, Henglin M, Kim A, Ebinger JE, Claggett B, Merz CNB, Cheng S. Sex differences in blood pressure associations with cardiovascular outcomes. *Circulation*. 2021;143:761–763. doi: 10.1161/CIRCULATIONAHA.120.049360
- Skurnick JH, Aladjem M, Aviv A. Sex differences in pulse pressure trends with age are cross-cultural. *Hypertension*. 2010;55:40–47. doi: 10.1161/HYPERTENSIONAHA.109.139477
- Purkiss S, Huckell VF. Cardiovascular physiology: similarities and differences between healthy women and men. *J SOGC*. 1997;19:853–859. doi: 10.1016/S0849-5831(97)80008-0
- Wiebe CG, Gledhill N, Warburton DE, Jamnik VK, Ferguson S. Exercise cardiac function in endurance-trained males versus females. *Clin J Sport Med*. 1998;8:272–279. doi: 10.1097/00042752-199810000-00004
- Chung AK, Das SR, Leonard D, Peshock RM, Kazi F, Abdullah SM, Canham RM, Levine BD, Drazner MH. Women have higher left ventricular ejection fractions than men independent of differences in left ventricular volume. *Circulation*. 2006;113:1597–1604. doi: 10.1161/CIRCULATIONAHA.105.574400
- Jang SY, Ju EY, Huh EH, Kim JH, Kim D-K. Determinants of brachial-ankle pulse wave velocity and carotid-femoral pulse wave velocity in healthy Koreans. *J Korean Med Sci*. 2014;29:798–804. doi: 10.3346/jkms.2014.29.6.798
- Vermeersch SJ, Rietzschel ER, De Buyzere ML, De Bacquer D, De Backer G, Van Bortel LM, Gillebert TC, Verdonck PR, Segers P. Age and gender related patterns in carotid-femoral PWV and carotid and femoral stiffness in a large healthy, middle-aged population. *J Hypertens*. 2008;26:1411–1419. doi: 10.1097/HJH.0b013e3282ffac00
- Denton KM, Hilliard LM, Tare M. Sex-related differences in hypertension. *Hypertension*. 2013;62:674–677. doi: 10.1161/HYPERTENSIONAHA.113.00922
- Tikkakoski AJ, Tahvanainen AM, Leskinen MH, Koskela JK, Haring A, Viitala J, Kähönen MAP, Kööbi T, Niemelä O, Mustonen JT, et al. Hemodynamic alterations in hypertensive patients at rest and during passive head-up tilt. *J Hypertens*. 2013;31:906–915. doi: 10.1097/HJH.0b013e32835ed605
- Esler M, Julius S, Coghlan B, Sari CI, Guo L, Esler D. Consequences of the evolutionary cardiovascular challenge of human bipedalism: orthostatic intolerance syndromes, orthostatic hypertension. *J Hypertens*. 2019;37:2333–2340. doi: 10.1097/HJH.0000000000002198

17. Reulecke S, Charleston-Villalobos S, Voss A, González-Camarena R, González-Hermosillo J, Gaitán-González MJ, Hernández-Pacheco G, Schroeder R, Aljama-Corrales T. Men and women should be separately investigated in studies of orthostatic challenge due to different gender-related dynamics of autonomic response. *Physiol Meas*. 2016;37:314–332. doi: 10.1088/0967-3334/37/3/314
18. Tahvanainen AM, Tikkakoski AJ, Koskela JK, Nordhausen K, Viitala JM, Leskinen MH, Kähönen MAP, Kööbi T, Uitto MT, Viik J, et al. The type of the functional cardiovascular response to upright posture is associated with arterial stiffness: a cross-sectional study in 470 volunteers. *BMC Cardiovasc Disord*. 2016;16:101. doi: 10.1186/s12872-016-0281-8
19. Magalhães P, Capingana DP, Silva ABT, Ferreira AVL, de Sá CR, Rodrigues SL, Mill JG. Age- and gender-specific reference values of pulse wave velocity for African adults: preliminary results. *Age*. 2013;35:2345–2355. doi: 10.1007/s11357-012-9504-9
20. Kangas P, Tahvanainen A, Tikkakoski A, Koskela J, Uitto M, Viik J, Kähönen M, Kööbi T, Mustonen J, Pörsti I. Increased cardiac workload in the upright posture in men: noninvasive hemodynamics in men versus women. *J Am Heart Assoc*. 2016;5:e002883. doi: 10.1161/JAHA.115.002883
21. Kangas P, Tikkakoski A, Kettunen J, Eräranta A, Huhtala H, Kähönen M, Sipilä K, Mustonen J, Pörsti I. Changes in hemodynamics associated with metabolic syndrome are more pronounced in women than in men. *Sci Rep*. 2019;9:1–11. doi: 10.1038/s41598-019-54926-0
22. Teivaanmäki T, Cheung YB, Pulakka A, Virkkala J, Maleta K, Ashorn P. Height gain after two-years-of-age is associated with better cognitive capacity, measured with Raven's coloured matrices at 15-years-of-age in Malawi. *Matern Child Nutr*. 2017;13:e12326. doi: 10.1111/mcn.12326
23. Maleta K, Virtanen SM, Espo M, Kulmala T, Ashorn P. Childhood malnutrition and its predictors in rural Malawi. *Paediatr Perinat Epidemiol*. 2003;17:384–390. doi: 10.1046/j.1365-3016.2003.00519.x
24. Maleta K, Virtanen S, Espo M, Kulmala T, Ashorn P. Timing of growth faltering in rural Malawi. *Arch Dis Child*. 2003;88:574–578. doi: 10.1136/adc.88.7.574
25. WHO. The world health report. <https://www.WHO.int/whr/2003/en/>. Accessed February 18, 2021.
26. Teivaanmäki T, Cheung YB, Kortekangas E, Maleta K, Ashorn P. Transition between stunted and nonstunted status: both occur from birth to 15 years of age in Malawi children. *Acta Paediatr*. 2015;104:1278–1285. doi: 10.1111/apa.13060
27. WHO child growth standards: length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: methods and development. <https://www.who.int/publications-detail-redirect/924154693X>. Accessed February 25, 2021.
28. de Onis M, Onyango AW, Borghi E, Siyam A, Nishida C, Siekmann J. Development of a WHO growth reference for school-aged children and adolescents. *Bull World Health Organ*. 2007;85:660–667. doi: 10.2471/BLT.07.043497
29. USAID-FANTA III. Household Food Insecurity Access Scale (HFIA) for Measurement of Food Access: Indicator Guide|Food and Nutrition Technical Assistance III Project (FANTA). <https://www.fantaproject.org/monitoring-and-evaluation/household-food-insecurity-access-scale-hfias>. Accessed October 18, 2021.
30. Machinjili C. Population and Housing Census Questionnaire 2008, Republic of Malawi, National Statistical Office. https://international.ipums.org/international-action/source_documents/enum_form_mw2008a_tag.xml#63. Accessed October 18, 2021.
31. Inker LA, Schmid CH, Tighiouart H, Eckfeldt JH, Feldman HI, Greene T, Kusek JW, Manzi J, Van Lente F, Zhang YL, et al. Estimating glomerular filtration rate from serum creatinine and cystatin C. *N Engl J Med*. 2012;367:20–29. doi: 10.1056/NEJMoa1114248
32. Gorlin R, McMillan IKR, Medd WE, Matthews MB, Daley R. Dynamics of the circulation in aortic valvular disease. *Am J Med*. 1955;18:855–870. doi: 10.1016/0002-9343(55)90169-8
33. Weiss W, Gohlisch C, Harsch-Gladisch C, Tölle M, Zidek W, van der Giet M. Oscillometric estimation of central blood pressure: validation of the Mobil-O-Graph in comparison with the SphygmoCor device. *Blood Press Monit*. 2012;17:128–131. doi: 10.1097/MBP.0b013e328333ff63
34. Weber T, Wassertheurer S, Rammer M, Maurer E, Hametner B, Mayer CC, Kropf J, Eber B. Validation of a brachial cuff-based method for estimating central systolic blood pressure. *Hypertension*. 2011;58:825–832. doi: 10.1161/HYPERTENSIONAHA.111.176313
35. Wei W, Tölle M, Zidek W, van der Giet M. Validation of the Mobil-O-Graph: 24 h-blood pressure measurement device. *Blood Press Monit*. 2010;15:225–228. doi: 10.1097/MBP.0b013e3283338892f
36. Franssen PM, Imholz BP. Evaluation of the Mobil-O-Graph new generation ABPM device using the ESH criteria. *Blood Press Monit*. 2010;15:229–231. doi: 10.1097/MBP.0b013e3283339b38
37. Hametner B, Wassertheurer S, Kropf J, Mayer C, Eber B, Weber T. Oscillometric estimation of aortic pulse wave velocity: comparison with intra-aortic catheter measurements. *Blood Press Monit*. 2013;18:173–176. doi: 10.1097/MBP.0b013e3283614168
38. CDC. Section "Functional-Assessments" on the web-page Clinical Resources|STEAD|CDC Injury Center 2021. <https://www.cdc.gov/stead/materials.html>. Accessed October 18, 2021.
39. Laurent S, Cockcroft J, Van Bortel L, Boutouyrie P, Giannattasio C, Hayoz D, Pannier B, Vlachopoulos C, Wilkinson I, Struijker-Boudier H; on behalf of the European Network for Non-invasive Investigation of Large Arteries. Expert consensus document on arterial stiffness: methodological issues and clinical applications. *Eur Heart J*. 2006;27:2588–2605. doi: 10.1093/eurheartj/ehl254
40. Wenner MM, Stachenfeld NS. Blood pressure and water regulation: understanding sex hormone effects within and between men and women. *J Physiol*. 2012;590:5949–5961. doi: 10.1113/jphysiol.2012.236752
41. Roman MJ, Devereux RB. Association of central and peripheral blood pressures with intermediate cardiovascular phenotypes. *Hypertension*. 2014;63:1148–1153. doi: 10.1161/HYPERTENSIONAHA.114.03361
42. Vlachopoulos C, Aznaouridis K, O'Rourke MF, Safar ME, Baou K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with central haemodynamics: a systematic review and meta-analysis. *Eur Heart J*. 2010;31:1865–1871. doi: 10.1093/eurheartj/ehq024
43. Sparrow D, Tift CP, Rosner B, Weiss ST. Postural changes in diastolic blood pressure and the risk of myocardial infarction: the Normative Aging Study. *Circulation*. 1984;70:533–537. doi: 10.1161/01.CIR.70.4.533
44. George J, Rapsomaniki E, Pujades-Rodriguez M, Shah AD, Denaxas S, Herrett E, Smeeth L, Timmis A, Hemingway H. How does cardiovascular disease first present in women and men? Incidence of 12 cardiovascular diseases in a contemporary cohort of 1 937 360 people. *Circulation*. 2015;132:1320–1328. doi: 10.1161/CIRCULATIONAHA.114.013797
45. Reulecke S, Charleston-Villalobos S, Voss A, González-Camarena R, González-Hermosillo J, Gaitán-González MJ, Hernández-Pacheco G, Schroeder R, Aljama-Corrales T. Orthostatic stress causes immediately increased blood pressure variability in women with vasovagal syncope. *Comput Methods Programs Biomed*. 2016;127:185–196. doi: 10.1016/j.cmpb.2015.12.005
46. Hamrefors V, Spahic JM, Nilsson D, Senneby M, Sutton R, Melander O, Fedorowski A. Syndromes of orthostatic intolerance and syncope in young adults. *Open Heart*. 2017;4:e000585. doi: 10.1136/openhrt-2016-000585
47. Ghariq M, Thijs RD, Bek LM, van Zwet EW, Benditt DG, van Dijk JG. A higher proportion of men than of women fainted in the phase without nitroglycerin in tilt-induced vasovagal syncope. *Clin Auton Res*. 2020;30:441–447. doi: 10.1007/s10286-020-00666-5
48. Raj SR, Ahmed SB, Sheldon RS. Understanding vasovagal syncope: a role for sex and gender. *Clin Auton Res*. 2020;30:369–370. doi: 10.1007/s10286-020-00689-y
49. Parati G, Ochoa JE, Lombardi C, Bilo G. Assessment and management of blood-pressure variability. *Nat Rev Cardiol*. 2013;10:143–155. doi: 10.1038/nrcardio.2013.1
50. Bakkar N-MZ, El-Yazbi AF, Zouein FA, Fares SA. Beat-to-beat blood pressure variability: an early predictor of disease and cardiovascular risk. *J Hypertens*. 2021;39:830–845. doi: 10.1097/HJH.0000000000002733
51. Frey MAB, Tomaselli CM, Hoffer WG. Cardiovascular responses to postural changes: differences with age for women and men. *J Clin Pharmacol*. 1994;34:394–402. doi: 10.1002/j.1552-4604.1994.tb04979.x
52. Shoemaker JK, Hogeman CS, Khan M, Kimmerly DS, Sinoway LI. Gender affects sympathetic and hemodynamic response to postural stress. *Am J Physiol Heart Circ Physiol*. 2001;281:H2028–H2035. doi: 10.1152/ajpheart.2001.281.5.H2028
53. Kulmala T, Vaahera M, Ndekha M, Koivisto AM, Cullinan T, Salin ML, Ashorn P. Gestational health and predictors of newborn weight amongst pregnant women in rural Malawi. *Afr J Reprod Health*. 2001;5:99–108. doi: 10.2307/3583328

54. Kulmala T, Vaahtera M, Ndekha M, Koivisto A-M, Cullinan T, Salin M-L, Ashorn P. The importance of preterm births for peri- and neonatal mortality in rural Malawi. *Paediatr Perinat Epidemiol*. 2000;14:219–226. doi: 10.1046/j.1365-3016.2000.00270.x
55. Bailey RC, Kamenga MC, Nsuami MJ, Nieburg P, St Louis ME. Growth of children according to maternal and child HIV, immunological and disease characteristics: a prospective cohort study in Kinshasa, Democratic Republic of Congo. *Int J Epidemiol*. 1999;28:532–540. doi: 10.1093/ije/28.3.532
56. Vaahtera M, Kulmala T, Ndekha M, Koivisto A-M, Cullinan T, Salin M-L, Ashorn P. Antenatal and perinatal predictors of infant mortality in rural Malawi. *Arch Dis Child Fetal Neonatal Ed*. 2000;82:F200–F204. doi: 10.1136/fn.82.3.F200
57. Waterlow JC, Nestlé Nutrition SA, eds. *Linear Growth Retardation in Less Developed Countries*. Nestlé Nutrition; Raven Press; 1988:1–295.
58. Rosengren A, Smyth A, Rangarajan S, Ramasundarahettige C, Bangdiwala SI, AlHabib KF, Avezum A, Bengtsson Boström K, Chifamba J, Gulec S, et al. Socioeconomic status and risk of cardiovascular disease in 20 low-income, middle-income, and high-income countries: the Prospective Urban Rural Epidemiologic (PURE) study. *Lancet Glob Health*. 2019;7:e748–e760. doi: 10.1016/S2214-109X(19)30045-2
59. Laslett LJ, Alagona P, Clark BA, Drozda JP, Saldivar F, Wilson SR, Poe C, Hart M. The worldwide environment of cardiovascular disease: prevalence, diagnosis, therapy, and policy Issues. *J Am Coll Cardiol*. 2012;60:S1–S49. doi: 10.1016/j.jacc.2012.11.002
60. Havranek EP, Mujahid MS, Barr DA, Blair IV, Cohen MS, Cruz-Flores S, Davey-Smith G, Dennison-Himmelfarb CR, Lauer MS, Lockwood DW, et al. Social determinants of risk and outcomes for cardiovascular disease: a scientific statement from the American Heart Association. *Circulation*. 2015;132:873–898. doi: 10.1161/CIR.0000000000000228
61. USAID-DHF-Program. Malawi Malaria Indicator Survey 2017. <https://dhsprogram.com/publications/publication-MIS28-MIS-Final-Reports.cfm>. Accessed October 18, 2021.
62. Vlachopoulos C, Aznaouridis K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. *J Am Coll Cardiol*. 2010;55:1318–1327. doi: 10.1016/j.jacc.2009.10.061
63. Schwartz JE, Feig PU, Izzo JL. Pulse wave velocities derived from cuff ambulatory pulse wave analysis: effects of age and systolic blood pressure. *Hypertension*. 2019;74:111–116. doi: 10.1161/HYPERTENSIONAHA.119.12756
64. Arterial Stiffness' Collaboration. Determinants of pulse wave velocity in healthy people and in the presence of cardiovascular risk factors: establishing normal and reference values. *Eur Heart J*. 2010;31:2338–2350. doi: 10.1093/eurheartj/ehq165
65. Sherwood A, Hughes JW, McFetridge J. Ethnic differences in the hemodynamic mechanisms of ambulatory blood pressure regulation. *Am J Hypertens*. 2003;16:270–273. doi: 10.1016/S0895-7061(02)03269-7
66. Light KC, Turner JR, Hinderliter AL, Sherwood A. Race and gender comparisons. I: hemodynamic responses to a series of stressors. *Health Psychol*. 1993;12:354–365. doi: 10.1037/0278-6133.12.5.354
67. Kelsey RM, Alpert BS, Patterson SM, Barnard M. Racial differences in hemodynamic responses to environmental thermal stress among adolescents. *Circulation*. 2000;101:2284–2289. doi: 10.1161/01.CIR.101.19.2284
68. Fernandes-Silva MM, Shah AM, Hegde S, Goncalves A, Claggett B, Cheng S, Nadruz W, Kitzman DW, Konety SH, Matsushita K, et al. Race-related differences in left ventricular structural and functional remodeling in response to increased afterload: the ARIC study. *JACC Heart Fail*. 2017;5:157–165. doi: 10.1016/j.jchf.2016.10.011
69. Duprez DA, Jacobs DR, Lutsey PL, Herrington D, Prime D, Ouyang P, Barr RG, Bluemke DA. Race/ethnic and sex differences in large and small artery elasticity – results of the multi-ethnic study of atherosclerosis (MESA). *Ethn Dis*. 2009;19:243–250.
70. Papaioannou TG, Xanthis D, Argyris A, Vernikos P, Mastakoura G, Samara S, Floros IT, Protogerou AD, Tousoulis D. Accuracy and precision of cardiac output estimation by an automated, brachial cuff-based oscillometric device in patients with shock. *Proc Inst Mech Eng*. 2020;234:1330–1336. doi: 10.1177/0954411919888321
71. Bikia V, Pagoulatou S, Trachet B, Soulis D, Protogerou AD, Papaioannou TG, Stergiopulos N. Noninvasive cardiac output and central systolic pressure from cuff-pressure and pulse wave velocity. *IEEE J Biomed Health Inform*. 2020;24:1968–1981. doi: 10.1109/JBHI.2019.2956604

SUPPLEMENTAL MATERIAL

Supplemental Methods

Data S1. Household Food Insecurity Access Scale (HFIAS) Generic Questionnaire²⁹

HFIAS

1. Did you worry that your household would not have enough food?
2. Were you or any household member not able to eat the kinds of foods you preferred because of a lack of resources?
3. Did you or any household member have to eat a limited variety of foods due to a lack of resources?
4. Did you or any household member have to eat some foods that you really did not want to eat because of a lack of resources to obtain other types of food?
5. Did you or any household member have to eat smaller meal than you felt you needed because there was not enough food?
6. Did you or any household member miss breakfast, lunch, or dinner because there was not enough food?
7. Was there ever no food to eat in your household because of lack of resources to get food?
8. Did you or any household member go to sleep at night hungry, because there was not enough food?
9. Did you or any household member go a whole day and night without eating because there was not enough food?

Example:

1. In the past four weeks, did you worry that your household would not have enough food?

0 = No

1 = Rarely (once or twice in the past four weeks)

2 = Sometimes (three to ten times in the past four weeks)

3 = Often (more than ten times in the past four weeks)

Data S2. Living Environment Questionnaire³⁰

1. What is the building material of the walls of the main house?

Options: straw/grass/mud, unburnt brick, burnt brick, other.

2. What is the roofing material of the house?

Options: grass, iron sheets or tiles, other/specify.

3. What is the main source of drinking water?

Options: lake, unprotected well, protected well, borehole, piped water, other/specify.

4. What kind of sanitary facilities does the household have?

Options: none, regular pit latrine, ventilated improved pit latrine, water closet, other/specify.

5. What kind of lights does the household have?

Options: none, candles, paraffin lamp, torch with batteries, car battery, mains cable, other/specify.

6. What is the main source of cooking fuel?

Options: self-collected firewood, purchased firewood, charcoal, electricity, other/specify.

The option 'other' was instructed to be specified by the participants.

Table S1. Altogether 429 subjects participated in the study, while successful blood pressure recordings and measurements of weight and height were available from 419 subjects. The numbers of subjects with missing information among these 419 participants are given below.

	Women	Men
Food insecurity data	8	8
Reading and writing	3	3
School years	3	3
Living environment data	3	3
Malaria test	2	2
Mean length-age-Z-score during the first 6 months	8	4
Plasma analyses	4	1
Hemoglobin	2	2
Upright hemodynamic values	3	2
Supine to upright changes of hemodynamic values	3	2