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ORIGINAL RESEARCH

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

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**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/m$^2$) 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

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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]

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## 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 |

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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 data[27] 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 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-Laroche Ltd, Basel, Switzerland). Estimated glomerular filtration rate was calculated using the Chronic Kidney Disease Epidemiology Collaboration creatinine-based formula.[31]

**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) |
| *Plasmodium falciparum*: 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.

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### *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×(mean aortic pressure–pulmonary artery occlusion pressure)×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 Society[35] and European Hypertension Society criteria.[36] Also, the evaluated PWV has been compared with tonometric devices and invasively obtained values.[37]

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### *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,

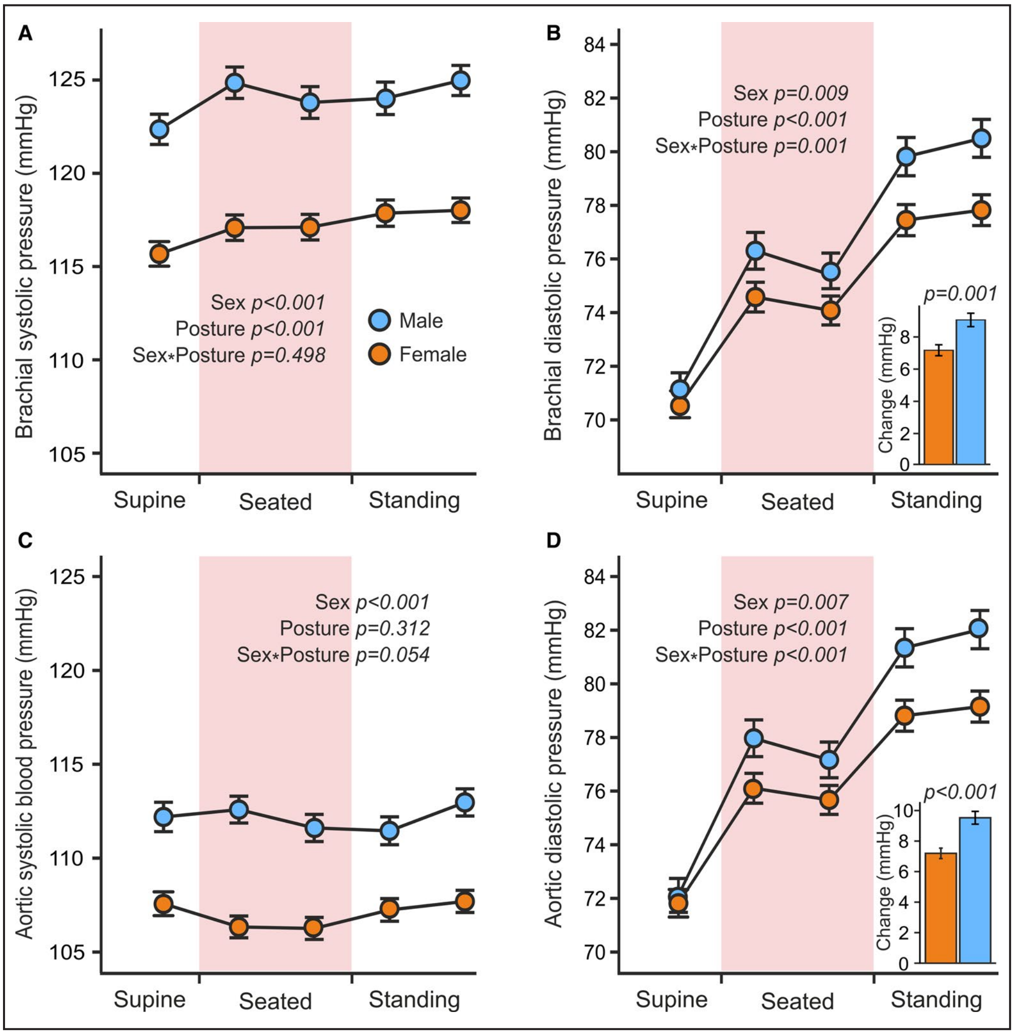


**Figure 1. Line graphs show brachial systolic (A) and diastolic (B) and aortic systolic (C) and diastolic (D) blood pressure values in 251 women and 168 men during supine, seated, and standing positions.**

**B** and **D**, Insets show the supine-to-upright increase in diastolic blood pressure; mean±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.

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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/m$^2$; $P=0.001$), but not supine-to-standing (−13.6±0.6 versus

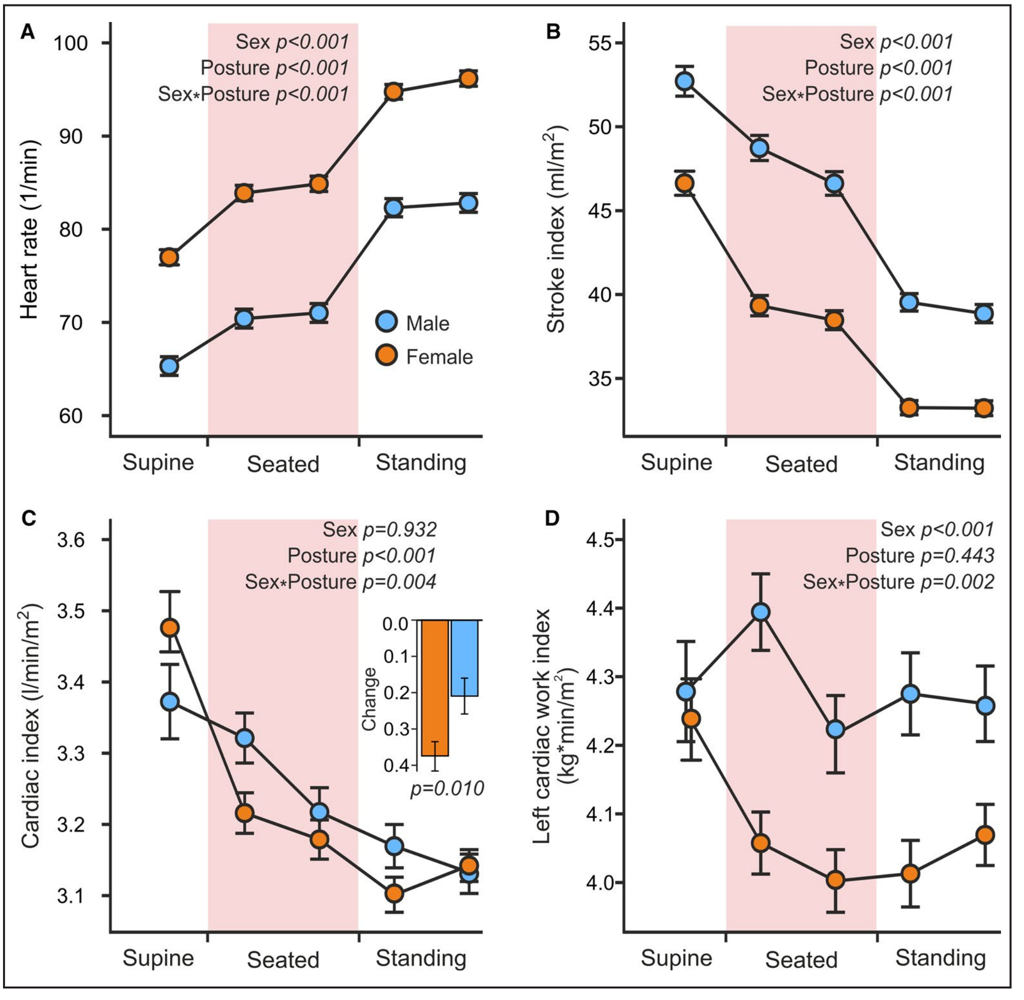


**Figure 2. Heart rate (A), stroke index (B), cardiac index (C), and left cardiac work index (D) in male and female participants.**
**C**, Inset shows the supine-to-upright decrease in cardiac index; statistics as in Figure 1.

–13.3±0.8 mL/m$^2$; $P$=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/m$^2$; $P$=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

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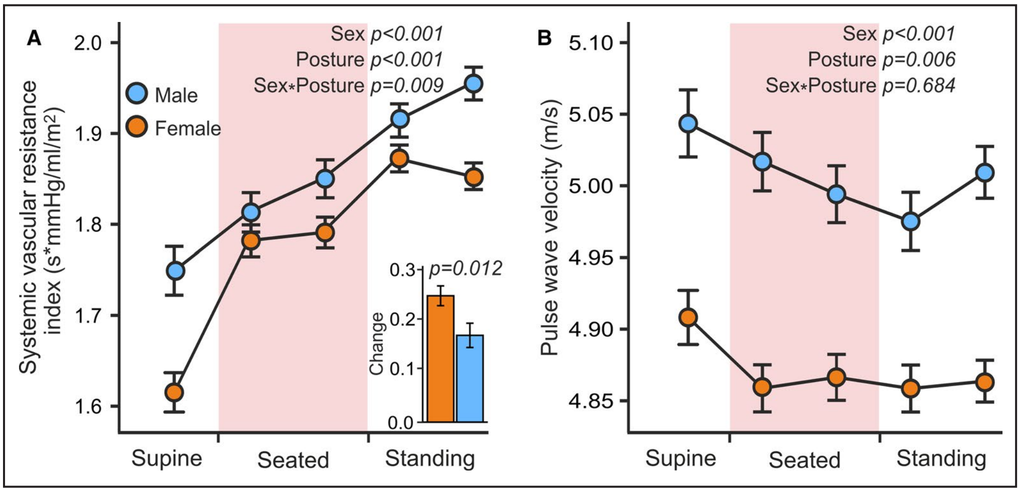


**Figure 3. Systemic vascular resistance index (A) and waveform-derived evaluation of pulse wave velocity (B) in male and female participants.**

**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

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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

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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.

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### Disclosures

None.

### Supplemental Material

Data S1–S2
Table S1

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# SUPPLEMENTAL MATERIAL

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## Supplemental Methods

## Data S1. Household Food Insecurity Access Scale (HFIAS) Generic Questionary[29]

### 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)

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**Data S2. Living Environment Questionary**[30]

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.

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**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 |

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