**Artigo Original**

**Lifestyle changes reduce central blood pressure in pre-hypertensive individuals**

**Resumo**

**Introdução:** A modificação do estilo de vida (MEV) influencia diretamente a pressão arterial periférica em indivíduos pré-hipertensos. O comportamento da pressão sistólica central (PSC) em relação à MEV não está plenamente conhecido. Além disso, a pré-hipertensão (PH) oferece risco cardiovascular semelhante ao de um hipertenso leve e pode estar associado com alterações da função endotelial alterando a PSC. **Objetivos:** Demonstrar a influência da MEV com exercício físico e dieta alimentar em parâmetros antropométricos e hemodinâmicos, incluindo a PSC, em indivíduos pré-hipertensos. **Métodos:** Foram estudados 56 pacientes com PH antes e após 3 meses de MEV. A PSC foi avaliada utilizando-se um sistema de tonometria da artéria radial antes e após a MEV. **Resultados:** A média de idade da população estudada foi 48±10,8 anos. Houve redução significativa na PAS (127±8,1 para 122±9,2; p=0,003), PAD (75±7,4 para 72±7,7; p=0,003), PAM (92±7,0 para 89±7,6; p=0,002), IMC (29,0±4,6 para 28,5±4,6; p=0,001) e na relação C/Q (0,91±0,07 para 0,89±0,06; p=0,0007) após 03 meses de MEV. Também se observou redução da PSC (113±10,7 para 107±10,9; p=0,0001) após três meses de MEV. **Conclusão:** AMEV promoveu melhora pressão arterial periférica e central de indivíduos pré-hipertensos.

**Palavras chaves:** pressão arterial, estilo de vida, rigidez arterial, pre-hipertensão, dieta dash.

**Abstract**

**Introduction:** Lifestyle changes (LC) influence peripheral blood pressure (BP) in pre-hypertensive (PH) individuals; the behavior of central systolic BP (CBP) in respect to LC is not fully known. However, pre-hypertension cardiovascular risk is similar to mild hypertension and can be associated with changes in the endothelial function thereby altering the CBP. **Objectives:** Thus, to demonstrate the influence of LC on the peripheral and the central blood pressure in PH individuals. **Methods:** 56 PH patients were studied before and after three months of LC (Dash diet and aerobic exercises). The CBP was measured by tonometry of the radial artery before and after LC. **Results:** The mean age of the study population was 48 ± 10.8 years. There were significant reductions in peripheral systolic pressure (127±8.1 vs. 122 ± 9.2, *P=0.003*), in the body mass index (29.0±4.6 vs. 28.5±4.6, *P=0.001*) and the waist:hip ratio(0.91 ± 0.07 vs. 0.89 ± 0.06, *P=0.0007*) and also in the CBP (113±10.7 vs. 107±10.9, *P=0.0001*) after three months of LC. **Conclusion:** Lifestyle changes promote improvement in peripheral and central BP in PH individuals.

**Key words:** blood pressure; lifestyle; arterial stiffness; pre-hypertension; dash diet.

**Introduction**

Systemic arterial hypertension (SAH) is the main risk factor in the development of cardiovascular disease (CVD), a major cause of mortality worldwide.1 Furthermore, pre-hypertension has a similar cardiovascular risk to mild hypertension2,3,4 and increases the subject’s chance of becoming hypertensive within a 10-yearspan.5

Although the peripheral arterial pressure is used more in the clinical practice to define both hypertension andpre-hypertension,6,7these measures do not reflect the central aortic pressure.8Recent evidence shows that the central blood pressure (CBP) has greater significance as a predictor of cardiovascular complications than the peripheral blood pressure (BP) measured in the brachial artery.9,6The importance of evaluating the CBP increased substantially with the publication of the Conduit Artery Function Evaluation study (CAFE). Under physiological conditions, the CBP is normally lower than the peripheral BP and many studies have demonstrated a consistent relationship between the CBP and cardiovascular mortality.10, 9 However, few studies demonstrate the behavior of the CBP in prehypertensive individuals. In turn, the augmentation index (AIx) is another parameter used for evaluating the central hemodynamic. It is also able to predict clinical outcomes for detecting the wave pulse reflection in the arterial tree.11,12The current standard measure to assess the central hemodynamic involves the non-invasive evaluation of the radial artery by applanation tonometry, including the CBP and an analysis of the AIx, which represents the increase in CBP due to reflected waves. Thus, the greater the amplitude of reflected waves, the greater the overload on the left ventricle and consequently higher CBP.13-16

On the other hand, lifestyle change (LC) is considered a therapeutic approach to treat hypertension. The two main LC action points are represented by the DASH (Dietary Approaches to Stop Hypertension) diet and physical exercise, which act by improving metabolic parameters and endothelial function.17-20, 2

Studies have shown that aerobic exercise of low to moderate intensity for 30 minutes at a frequency of at least five times per week, significantly reduces the peripheral and central BP and significantly improve endothelial function in hypertensive patients.21,22 However, the effects of LC in the AIx and CBP need to be better investigated in pre-hypertensive subjects. Thus, the present study sought to demonstrate the influence of LC on the anthropometric and hemodynamic (peripheral and central) parameters of pre-hypertensive individuals.

**Methods**

This was a cohort, randomized, paired, prospective study, which evaluated 56 prehypertensive individuals of both genders aged between 30 and 70 years. Prehypertension was defined by office BP values between 120 and 139 mmHg for systolic blood pressure (SBP) and/or between 80 and 89 mmHg for diastolic blood pressure (DBP).For this characterization was considered the mean of three BP measurements.2The exclusion criteria were low life expectancy, previous use of antihypertensive medications, cardiovascular disease and pregnancy. All study participants completed a standard questionnaire to assess risk factors and were extensively informed about the nature of the study. The study was approved by the *Ethics Committee of the institution (protocol 2205/2009)*and all participants gave their written informed consent.

**Clinical evaluation**

All volunteers underwent clinical evaluations, physical examinations and an investigation of their living habits. Participants were instructed not to use any medication and not to ingest alcoholic beverages within 24 hours leading up to the evaluation. Blood pressure was measured in the office using a digital sphygmomanometer according to the VII Brazilian Guidelines on Hypertension Treatment.2The body mass index (BMI) was calculated using the formula weight divided by height squared (kg/m2).The examination was performed with the subjects not wearing shoes and wearing light clothing. A calibrated digital scale was used to measure the weight. The height and waist circumference were measured in centimeters using a tape measure; measurement of the waist was performed at the mid-point between the anterior superior iliac crest and the lowest rib at the end of expiration.23,24

**Biochemical tests**

Blood samples were drawn after 12 h of fasting to measure total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), triglycerides (TG), glycemia, glycated hemoglobin, uric acid, serum creatinine and potassium. Microalbuminuria was also evaluated from urine samples collected during 24 hours and determined using the nephelometric method. The glomerular filtration ratio (GFR) was estimated using the MDRD (Modification of Diet in Renal Disease) and CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) formula.25,26

Serum cholesterol was evaluated according to the Brazilian Guidelines for Dyslipidemias.20 Low-density lipoprotein cholesterol (LDLc) was calculated using the Friedewald formula for patients with triglycerides levels below 400 mg/dL (LDLc = TC − HDLc − TG/5).2

**Evaluation of central systolic blood pressure and augmentation index**

CSP and AIx measurements were carried out by a non-invasive technique using applanation tonometry of the radial artery (HEM9000AI device, OMRON Healthcare Co. Kyoto, Japan).

The patient was instructed to fast (no alcohol or any kind of stimulant, or smoking) for at least four hours before arriving at the office. Moreover, the subject’s bladder should be empty. The patient was placed in a quiet, comfortable environment (temperature between 21°C and 24°C),and the parameters measurement was taken in the setting position after 5 to 10 minutes of rest prior to the test.2

Analysis of CBP and AIx was performed simultaneously with verification of the peripheral blood pressure, using a calibrated device and a correct size of pressure cuff, which should have an appropriate width to arm circumference ratio of 1:2. As table blood pressure is required before starting applanation tonometry. Stability was confirmed when the differences between two consecutive blood pressure measurements did not exceed 10 mmHg and 5 mmHg for SBP and DBP, respectively. The core parameters (CBP and AIx) were assessed once pressure stability was obtained. For this, the left forearm was supported on the equipment and the radial artery was palpated. Subsequently, a pressure sensor was placed on the artery and the hemodynamic parameters were read three times at three-minute intervals. For the test to be considered reliable, the standard deviation of the three tests should not exceed 10%. Functional hemodynamic tests and guidance on the LC were carried out in a specialized outpatient clinic.

**Research Protocol**

Blood for biochemical tests was drawn from patients who met the study criteria and they were submitted to peripheral (SBP and DBP) and central (CSP and AIx) hemodynamic assessments. After biochemical and functional hemodynamic evaluations, individuals received guidance regarding LC, which included the DASH diet (major food groups, proper portions and reduced sodium), physical activity (mainly aerobic) and healthy life habits (smoking cessation, reduced alcohol consumption and guidelines involving the adequate control of blood pressure).After 12 weeks of counseling on LC, repeat biochemical, and peripheral and central hemodynamics (CSP and AIx) evaluations were performed in order to verify the influence of LC on these parameters. Guidance on the DASH diet and physical activity were performed by a nutritionist and a physiotherapist, respectively.

The recommendations carried out aimed at minimizing the possible intervention in the daily food and physical life of the patients, so that they expressed the reality with the modification of the lifestyle in only one visit.

**Statistical analysis**

The descriptive statistical analysis of qualitative and quantitative variables were calculated from measures of central tendency, dispersion and frequency. Inferential analyses were performed by applying the *Kolmogorov-Smirnov* normality test and homoscedasticity *Levene test*. The paired t-test was used considering the nature of the data. Correlation analyses were performed using the Pearson method. Multiple logistic regression was used to check possible associations between hemodynamic and anthropometric responses and CSP. The Prism statistics program was used to perform the analysis. An alpha error of 5% was considered acceptable.

The sample size was calculated using the GraphPadStat Mate 2.0 program. The calculated sample size using a p-value of 0.05 and statistical power of 80% to detect a difference in central systolic pressure before and after LC of 6.06 mmHg was 50 individuals.

**Results**

The baseline demographic characteristics and habits are described in Table 1.There was a predominance of males and Caucasians, with most pre-hypertensive individuals consuming alcohol and reporting routine physical exercise.

**Table 1: Demographic characteristics and habits.**

|  |  |
| --- | --- |
|  | **Pre-hypertensive patients**(n = 56) |
| Age (years) – mean ± SD | 50.1 ± 10.9 |
| Gender (♂ / ♀) - n | 37/19 |
| Caucasian/Afro-descendant - n | 51/5 |
| Smoker - % | 15 |
| Alcohol consumption - % | 70 |
| Physical exercise - % | 71 |

SD: Standard deviation

Table 2 shows the anthropometric parameters and the peripheral and central hemodynamic values before and after LC. Statistically significant reductions in BMI and waist-hip ratio were observed. Note the statistically significant reductions in the systolic, diastolic and mean blood pressures and the CSP in pre-hypertensive patients after three months of LC (Table 2 and Figure 1).The AIx and AIx-75% reduced but not significantly (Figure 2).Moreover, reductions in the levels of glycated hemoglobin and plasma HDL-c were observed (Table 3). There were no statistically significant changes in respect to the other biochemical variables.

**Table 2: Anthropometric parameters, peripheral and central hemodynamic responses and arterial stiffness before and after lifestyle changes.**

|  |
| --- |
| **Pre-hypertensive patients** |
|  | **Before LC** | **After LC** | ***p-value*** |
| Weight (kg) | 81.0 ± 14.9 | 80.2 ± 14.5 | *NS* |
| BMI (kg/m2) | 29.0 ± 4.6 | 28.5 ± 4.6 | *0.001* |
| Waist (cm) | 103.5 ± 9.1 | 102.9 ± 9.2 | *NS* |
| Hips (cm) | 103.6 ± 8.8 | 103 ± 8.9 | *NS* |
| Waist/Hips (cm) | 0.91 ± 0.07 | 0.89 ± 0.06 | *0.0007* |
| **Peripherals parameters** |
| SBP (mmHg) | 127 ± 8.17 | 122 ± 9.25 | *0.003* |
| DBP(mmHg) | 75 ± 7.47 | 72 ± 7.72 | *0.003* |
| MBP(mmHg) | 92 ± 7.09 | 89 ± 7.65 | *0.002* |
| PP(mm Hg) | 52 ± 6.57 | 51 ± 6.77 | *NS* |
| HR(bpm) | 73± 11.2 | 73 ± 10.6 | *NS* |
| **Central parameters** |  |  |  |
| AI(%) | 82 ± 14.7 | 80 ± 14.6 | *NS* |
| AIx(%) | 82 ± 14.4 | 80 ± 14.7 | *NS* |
| CSP(mmHg) | 113 ± 10.7 | 107 ± 10.9 | *0.0001* |

Values are expressed as means ± SD. \* Significance p-value <0.05; Paired T-test; LC: lifestyle changes; BMI: body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MBP: Mean blood pressure; PP: Pulse pressure; HR:Heart rate; Aix: Augmentation Index; CSP: Central systolic pressure.

**Table 3: Biochemical parameters before and after lifestyle modification.**

|  |  |  |
| --- | --- | --- |
|  | **Pre-hypertensive patients** |  |
|  | **Before LC** | **After LC** | ***p-v*alue** |
| Fasting glycemia (mg / dL) | 92 ± 13.2 | 91 ± 14.0 | *NS* |
| HbA1c *(%)* | 5.6 ± 0.45 | 5.3 ± 0.44 | *0.04* |
| Total Cholesterol (mg / dL) | 205 ± 31.5 | 199 ± 33.7 | *NS* |
| HDL cholesterol (mg / dL) | 51.1 ± 9.77 | 45 ± 11.2 | *0.02* |
| LDL-cholesterol (mg / dL) | 127 ± 30.7 | 126 ± 33.6 | *NS* |
| Triglycerides (mg / dL) | 130 ± 55.5 | 151 ± 132.1 | *NS* |
| Creatinine (mg / dL) | 0.93 ± 0.20 | 2.7 ± 12.7 | *NS* |
| Potassium (mEq / dl) | 4.4 ± 0.46 | 4.6 ± 0.67 | *NS* |
| Uric acid (mg / dl) | 5.45 ± 1.37 | 5.96 ± 1.63 | *NS* |
| Microalbuminuria*(mg/24h)* | 20 ± 63.12 | 7.63 ± 6.35 | *NS* |
| **Glomerular Filtration Rate** |
| CKD-EPI*(mL/min)* | 90.5 ± 12.7 | 93.5 ± 17.9 | *NS* |
| MDRD*(mL/min)* | 90.3 ± 17.0 | 97.0 ± 35.2 | *NS* |

Values are expressed as means ± SD. \*Significant p-value<0.05; Paired t-test; HbA1c: glycated hemoglobin; HDL: High density lipoprotein; LDL: Low density lipoprotein; CKD-EPI - Collaboration of Epidemiological Chronic Kidney Disease; MDRD - Diet Modification in Renal Disease.

Figure 3 shows a multivariate correlation between the MBP and the CSP; there was a moderate correlation between the two measurements before and after LC, which demonstrates that central blood pressure is directly influenced by peripheral hemodynamics.

**Figure 1:** Comparison of peripheral hemodynamic responses (SBP, DBP, MBP, PP) before and after lifestyle changes (LC) in pre-hypertensive patients. SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: Mean Arterial Pressure; PP: Pulse Pressure



**Figure 2:** Comparison of the central hemodynamic response (PSC) and arterial stiffness (AI and AI-75) before and after lifestyle changes (LC) in pre-hypertensive patients. The middle bar represents the mean value. PSC: Central systolic pressure; AI: Augmentation Index.



**Figure 3:** Analysis of the Pearson multivariate correlation between CSP and MBP before and after lifestyle changes (LC). PSC – Central systolic pressure. MAP – Mean blood pressure.

**Discussion**

In this study, pre-hypertensive subjects had reductions in both BMI and waist-hip ratio in addition to the CSP, showing that the diet and physical exercise were effective in improving the anthropometric profile and thus reducing cardiovascular risk27 and the risk of developing metabolic syndrome (MS).28,29 Prevention of MS gives additional protection to arterial vascular health as oxidative stress associated with MS may cause imbalances in the regulation system for the production of free radicals.30

The BMI and waist/hip ratio, apart from being inexpensive techniques as initial examinations, are indicators of visceral adiposity, insulin resistance and hepatic steatosis.31LC, in particular exercise and diet, are the first non-pharmacological treatment option to control blood pressure and MS variables in pre-hypertensive patients.2,29

Different types of physical exercise and diet (DASH) offer significant benefits to pre-hypertensive and hypertensive individuals.32, 2,29These benefits can be found mainly in the parameters of arterial stiffness, and according to our findings, the CSP. Guimarães *et al.* tested different types of aerobic exercises (interval and continuous) supervised for a period of four months in 43 sedentary mild hypertensive subjects. Of these, 16 were allocated to the interval exercise group, 16 to the continuous exercise group and 11 to the control group. Maximum reductions in blood pressure and peripheral arterial stiffness, as demonstrated by an analysis of the pulse wave velocity, were seen mainly in the interval exercise group.33

The results of this study demonstrate reductions in peripheral blood pressure of pre-hypertensive patients submitted to LC. These data are consistent with data published in the literature.34, 35, 2, 29Márquez-Celedonio *et al.* studied 81 pre-hypertensive patients for six months, only 38 of whom were submitted to LC (diet, physical exercise and counselling to strengthen LC).The group submitted to LC had reductions of 9 mmHg and 14 mmHg in SBP at the end of three and six months of follow-up, respectively and the DBP decreased by 8 mmHg and 11 mmHg, respectively.36Interestingly, in that study the participants were followed up for a period of six months, while in the current study, subjects were submitted to LC for just three months with no subsequent follow-up visits. This suggests that perhaps a longer period of LC with counseling to strengthen the LC is necessary to obtain greater benefits. In addition, the participation of a multidisciplinary team with monitoring and periodic reinforcement would increase the chance of maintaining the changes over a longer period.

Diet and exercise are very important to change the lifestyle. Similar to food, exercise has a dose-dependent effect on the blood pressure. In addition, the effects of exercise on blood pressure are directly dependent on the recruited metabolic pathway. Only aerobic exercise used to be considered effective in reducing peripheral and central blood pressures however, resistance exercises also reduce blood pressure in pre-hypertensive individuals. Beck *et al.* analyzed 43 pre-hypertensive patients subjected to resistance training (opposing force) and endurance exercises (aerobic - 65% to 85% of maximum heart rate for a long time) three times a week for one hour per day over two months. There were no changes in the peripheral or central parameters of the control group. However, reductions of up to 9 mmHg in peripheral SBP and 8 mmHg in the peripheral DBP were recorded for the group that performed resistance training. Moreover, reductions of10 mmHg were obtained for the aortic systolic pressure and 7 mmHg for the aortic diastolic pressure. Reductions of 12 and 11 mmHg in the central and peripheral systolic pressures, respectively and 7 mmHg for both central and peripheral diastolic pressures were obtained in the group performing endurance exercises. In addition to the pressure coefficients, there was an improvement in arterial stiffness evidenced by a 10% reduction in carotid-radial pulse wave velocity and 11% in the femoral-artery, both in the resistance training and endurance groups.35The present study also demonstrated reductions in the CSP however the pulse wave velocity was not evaluated. The reduction in CSP can be explained by a possible reduction in peripheral arterial resistance generated by an increase in nitric oxide bioavailability and, consequently, greater vasodilation.37The vasodilator effect caused by the increase in NO bioavailability can be achieved regardless of any decrease in arterial stiffness, as a longer time of LC with a correct variety of physical exercise and diet is required to observe reductions in arterial stiffness. The same effects can also be observed with antihypertensive agents with vasodilator properties.38

So even with the limitations of duration of LC (three months), they were effective in reducing not only the peripheral pressure parameters (SBP, DBP and MAP), but also the CSP. Reductions of up to 2 mmHg in the peripheral SBP may reduce the risk of mortality from coronary ischemia by 7% and cerebrovascular disease by 10%.1 Moreover, the evaluation of CSP is important because it provides better risk assessment of cardiovascular morbidity and mortality equal to or better than the peripheral SBP.9This is because the CSP is mainly influenced by structural, and microvascular and macrovascular functional conditions.39The CSP is influenced directly by arterial stiffness or peripheral resistance and if it is altered, it increases cardiac work by increasing the after load in the left ventricle, favoring the development of myocardial hypertrophy and, consequently, heart failure, ischemic cardiac disease and arterial vascular remodeling.40

Another arterial stiffness parameter assessed by AIx did not show significant changes in the pre-hypertensive group before and after LC.

These results are similar to those obtained by Monteiro *et al.*, who conducted a meta-analysis of 14 studies involving prehypertensive and hypertensive patients. The authors found no changes in the behavior of arterial stiffness before and after aerobic exercises over four weeks or more.34

These findings emphasize the fact that the central blood pressure may be strongly influenced by the peripheral vascular resistance (microvessels), which was reduced with LC, thereby causing a reduction in arterial stiffness in pre-hypertensive patients. However, structural changes in the arterial wall would be required before observing changes in the AIx.34A longer period of LC with a variation in the dosage of exercise would be needed to see changes in the arterial wall structure. However, in this study, although the AIx was not reduced, the decrease in CSP was evident, which is a protective factor for hypertensive individuals. It is known that the disproportion between the peripheral and central blood pressures can be a cardiovascular risk regardless of other risk factors for cardiovascular disease.41, 39

The pre-hypertensive group had reductions in the glycated hemoglobin levels only, with the other biochemical parameters remaining unchanged. This positive change could be attributed to factors such as increased sensitivity to insulin, the GLUT-4 expression in the liver,42capillary density43and ability to oxidize free fatty acids.44In fact, Qiu *et al.* evaluated 16 studies involving glycemic behavior with aerobic resistance exercise and found that only walking was able to reduce glycated hemoglobin significantly.45

**Limitations of the study**

This study has several limitations. These included the lack of a control group in the study design, the duration of LC and monitoring of LC. The lack of a control group, in our view, was the main limitation. However, we used the group studied as a control of itself. Another limitation refers to the duration of LC. Perhaps if patients were exposed to LC for more time, we would have observed changes in the AIx of pre-hypertensive patients. Finally, there was no monitoring of the LC and hence there is no certainty that the subjects assiduously adhered to the LC. In addition, there were no corrections in the doses of exercise or diet.

**Conclusions**

Changing the life style related to diet and exercise was effective in reducing the BMI, the waist-hip ratio and peripheral (SBP, DBP, MAP) and central blood pressures in pre-hypertensive individuals.

**Conflicts of interest**

The authors of this study state no conflict of interests.

## Funding Statement

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