Higher Mean Blood Pressure is Associated With Autonomic Imbalance But Not With Endothelial Dysfunction in Young Soccer Players

Walter Vargas,1 Thiago Dipp,3 Rodrigo D.M. Plentz,2,3 and Katya Rigatto1

BACKGROUND
Blood pressure (BP) should be kept within a narrow range to allow adequate tissue perfusion. In particular, heart-rate variability (HRV) can be used to assess autonomic cardiovascular modulation, and flow-mediated dilation (FMD) can provide valuable information about the ability of the cardiovascular system to adapt to different pressures. Our objective in the study described here was to investigate the effect of a difference of 10 mm Hg in mean arterial pressure (MAP) on endothelial function and autonomic balance in young and normotensive soccer players.

METHODS
Twenty-nine young male soccer players (mean age 17.7 years) were divided into two groups according to their MAP (mm Hg): MAP-84 and MAP-94. The BP, FMD, HRV and maximum oxygen uptake (VO2max) of each group were measured.

RESULTS
Systolic BP (SBP) and diastolic BP (DBP) were significantly higher (P < 0.0001 and P < 0.006, respectively) in the MAP-94 group. There were no differences in VO2max and endothelial function in the two groups (P < 0.7699). However, the standard deviation (SD) of normal RR intervals (SDNN) and the square root of the mean squared differences in successive RR intervals (RMSSD) were significantly lower in the MAP-94 than in the MAP-84 group (P < 0.0001 and P < 0.005, respectively). In the MAP-94 group, both the high-and low-frequency components were significantly (P < 0.001, P < 0.021, P < 0.017, respectively) lower in both absolute and normalized units, whereas the LF/HF ratio was significantly (P < 0.012) higher.

CONCLUSIONS
Collectively, our findings indicate that in young soccer players, autonomic cardiovascular modulation is impaired when MAP is increased by 10 mm Hg, even within an optimal range of BP and regardless of endothelial function and VO2max.

Keywords: autonomic nervous system; heart rate variability; endothelial function; hypertension; blood pressure.

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There is a consensus that blood pressure (BP) should be kept within a narrow range to allow adequate tissue perfusion.1 It is very well established that cardiovascular risk factors are dependent on systemic arterial BP and that each millimeter of mercury increase in BP further increases the risks for cardiovascular events, including that for cardiovascular mortality.2,3 An increase in diastolic BP (DBP) is associated with an increase in the vascular resistance of small arterioles, whereas an increase in systolic BP (SBP) may indicate a decrease in arterial compliance.4,5 One mechanism of BP control is the carriage by peripheral afferents of BP information to the central nervous system, thus altering sympathetic and parasympathetic tone and thereby changing the heart rate (HR) and contributing to BP stabilization.6 For the past few decades, heart-rate variability (HRV) has been used as a valuable noninvasive tool for assessing autonomic modulation of the cardiovascular system.7 In sports medicine, HRV has also been used to evaluate the physical state of athletes and to identify their anaerobic thresholds.8

Numerous epidemiological data indicate that physical exercise is associated with beneficial changes in BP levels and that exercise is a healthy method by which to prevent9 and even control cardiovascular disease. The benefits of aerobic training include increases in parasympathetic modulation and baroreflex sensitivity, and relative decreases in sympathetic tone.10,11 In healthy young subjects, there is also consistent evidence that enhanced parasympathetic activity is associated with an increase in maximal oxygen uptake (VO2max).11

There is no doubt expressed in the literature that aerobic exercise is also essential for improving fitness and that exercise has favorable effects on BP and endothelial function.12–14 The regional distribution of blood flow is essential for regulating the contraction and relaxation of vascular endothelial smooth-muscle cells. Many blood vessels dilate in response...
to an increase in shear stress, which occurs during physical exercise. This phenomenon is called flow-mediated vasodilation (FMD) and can provide valuable information about the cardiovascular system's ability to adapt to the different pressures imposed on the system.

Considering the positive associations between physical fitness, represented by VO\textsubscript{2max} and endothelial function, and between VO\textsubscript{2max} and parasympathetic modulation, the following question must be addressed: What influence does BP have on these parameters when there is no evidence of impaired control of BP? Answering this question might contribute to the development of an early marker of “subclinical” cardiovascular disease. We therefore conducted a study to investigate the effect of a difference of 10 mm Hg in mean arterial pressure (MAP) on both endothelial function and autonomic balance in young and normotensive soccer players. Our goal was to evaluate the relationship among autonomic balance, VO\textsubscript{2max} and endothelial function in these soccer players according to their baseline BP.

**METHODS**

The study was approved by the ethics committee of the Universidade Federal de Ciências da Saúde de Porto Alegre. Twenty-nine young male soccer players (age 17 ± 2 years) participated in the study. All of the players had at least 3 years of prior soccer-specific training and lived in club accommodations with all meals provided equitably. The soccer players’ BP and autonomic and endothelial function were measured and they underwent exercise tests and anthropometric evaluation.

**Study design**

The data used in the study were collected during the soccer preseason, when the athletes were training but not participating in active competition. Before data collection, the athletes were fully informed about the research and tests to be performed in the study, after which they provided written informed consent to participate in it. The athletes were instructed to attend the Clinic Research Laboratory of the Instituto de Cardiologia do Rio Grande do Sul at 7 AM and to fast beforehand. The measurements made in the experimental sequence were, in sequential order: BP and HR, followed by measurements used to evaluate arterial endothelial function. One week later, anthropometric measurements were made (height, weight, age, body fat percentage, and time of training), and VO\textsubscript{2max} was estimated. This sequence was chosen to avoid interference among the measurements. The median SBP was used as a cutoff value to identify two distinct groups among the athletes in the study. Their respective mean arterial pressure (MAP) was used to identify the groups, with one group having an MAP of 84 mm Hg (MAP-84) and the other an MAP of 94 mm Hg (MAP-94).

**Blood pressure measurement**

Blood pressure was measured using the auscultatory method with calibrated equipment. The athletes were kept in a quiet environment for at least 5 minutes before their BP was measured, with their feet on the ground and their right arms supported at heart level. The BP cuff covered at least 80% of the upper arm. To confirm the data for each athlete, the BP measurement was repeated at least twice at 2-minute intervals. When a difference of more than 6 mm Hg was detected in two successive measurements, the measurements were repeated until the difference was less than 4 mm Hg. An average of two measurements was used for the classification of SBP.

**Heart-rate variability**

A Polar model RS800CX heart-rate monitor (Polar Electro Oy, Kempele, Finland), was used for collecting heart-rate data. The athletes were instructed to lie quietly in the supine position on a stretcher for the evaluation of HRV. The strap of the heart-rate monitor was secured around the chest to record a signal for 10 minutes with each athlete at rest in the supine position and for 10 minutes with the athlete standing in front of the stretcher. The signal was automatically stored as an RR interval and analyzed with Kubios HRV software version 2.0 (University of Kuopio, Kuopio, Finland). A 1,000-Hz sampling rate was chosen to provide a temporal resolution of 1 ms for each RR interval, a standard deviation (SD) of normal RR intervals (SDNN; ms), and the square root of the mean squared differences between consecutive RR intervals (RMSSD; ms).

An autoregressive method was used to determine HRV, on the basis of the spectral power integrated in two frequency bands: (i) a high-frequency (HF) band from 0.15–0.4 Hz; and (ii) a low-frequency (LF) band from 0.03–0.15 Hz. The results were expressed in absolute values (HFa and LFa; ms\textsuperscript{2}) and as respective percentages of these values (HFnu and LFnu; %). The LF/HF ratio, based on LFa and HFa, was then calculated as a last step.

**Assessment of endothelial function**

Endothelial function was assessed noninvasively by means of a brachial artery ultrasound probe (EnVisor Series, Philips Ultrasound, Bothell, WA) and Doppler ultrasonography using an instrument equipped with a 7- to 12-MHz high-resolution linear probe (L12-3, Philips, Bothell, WA, USA). The ultrasonography was performed in a silent, temperature-controlled laboratory room. The diameter of the left brachial artery was measured from B-mode ultrasound images at rest and during reactive hyperemia. A resting scan was performed before BP cuff inflation (50 mm Hg above SBP); when inflated, the cuff, which was placed around the forearm, occluded arterial flow for 5 minutes. This procedure causes ischemia and a consequent vasodilation via autoregulatory mechanisms. A second continuous scan was recorded from 30–120 seconds after cuff deflation. All of the ultrasound scans were performed and analyzed by the same experienced sonographer, who had no information about the subjects. The vessel diameter was measured offline at a fixed position with ultrasonic calipers at end-diastole, and incident with the R wave on a continuously recorded electrocardiogram. The dilatation was obtained by the difference from base line and after 10-second intervals during the period from 30–180 seconds. The value of FMD(%) indicates...
the increase in blood flow after release of the sphygmomanometer cuff.\textsuperscript{15}

### Maximal oxygen uptake

The Yo-Yo intermittent recovery test level 1 (Yo-Yo IR1)\textsuperscript{20} was used to assess VO\textsubscript{2max}. The athletes performed 2 × 20-minute shuttle runs at increasing speeds, interspersed with a 10-second period of active recovery. The test was controlled by audio signals from a compact-disc player and ended when the athlete was unable to maintain the speed for the test. The distance traveled at that point was the result of the test, as described by Bangsbo et al.\textsuperscript{20} For the calculation of VO\textsubscript{2max}, the following formula was used:

\[
\text{VO}_{2\text{max}} (\text{ml/min/kg}) = \text{IR1 distance (meters)} \times 0.0084 + 36.4
\]

### Statistical analysis

A median value was calculated to determine the SBP cutoff value for dividing the athletes into two groups. The normality and equality of variance of the data were assessed through the Shapiro–Wilk and Levene tests. The data were compared through the use of Student’s “t”-test or the Mann–Whitney U test, respectively. All analyses were done with SPSS software version 10.0 (SPSS Inc., Chicago, IL). The association between variables was assessed through Pearson correlations. The data are presented as means ± SD or, when stated, means ± SE. A value of \( P < 0.05 \) was considered statistically significant.

### RESULTS

#### Anthropometric measurements

There were no significant differences between the two study groups regarding to age (MAP-84 = 17.7 ± 1.0 years and MAP-94 = 17.6 ± 1.5 years; \( P = 0.1034 \)), weight (MAP-84 = 69.8 ± 4.1 kg, MAP-94 = 67.4 ± 4.1 kg; \( P = 0.5507 \)), or height (MAP-84 = 175 ± 5.2 cm, MAP-94 = 170 ± 7.2 cm; \( P = 0.9619 \)).

#### Measurements of systolic and diastolic blood pressure and maximal oxygen uptake

As expected, SBP and DBP (122 ± 4 mm Hg and 80 ± 4 mm Hg, respectively) were significantly (\( P < 0.005 \)) higher in the MAP-94 group than in the MAP-84 group (106 ± 6 mm Hg and 74 ± 6 mm Hg, respectively). There was no significant (\( P < 0.7699 \)) difference in VO\textsubscript{2max} (ml/min/kg) in the two groups, indicating that the physical fitness of the athletes in the groups was similar (MAP-94: 52 ± 2.6 ml/kg/min; MAP-84: 52 ± 2.2 ml/kg/min; \( P < 0.7699 \)).

#### Evaluation of heart-rate variability

The HRV in the time domain examined in the study, as measured by SDNN and RMSSD, was significantly lower in the MAP-94 than in the MAP-84 group. No significant differences in heart rate were observed between subjects in a supine position and when they were standing still (Table 1).

### Table 1. Heart rate and time-domain and frequency-domain measurements of resting heart-rate variation

<table>
<thead>
<tr>
<th></th>
<th>MAP-84 (n = 15)</th>
<th>MAP-94 (n = 14)</th>
<th>( P^a )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting HR, bpm</td>
<td>51±5</td>
<td>56±10</td>
<td>0.133</td>
</tr>
<tr>
<td>Standing HR, bpm</td>
<td>78±8</td>
<td>75±13</td>
<td>0.494</td>
</tr>
<tr>
<td>SDNN, ms</td>
<td>219±35</td>
<td>130±62</td>
<td>0.0001</td>
</tr>
<tr>
<td>RMSSD\textsuperscript{d}, ms</td>
<td>83±7.8</td>
<td>38.6±11.5</td>
<td>0.006</td>
</tr>
<tr>
<td>HFa\textsuperscript{b}, ms\textsuperscript{2}</td>
<td>3378±545</td>
<td>515±808</td>
<td>0.001</td>
</tr>
<tr>
<td>HFnlu</td>
<td>53±11</td>
<td>40±14</td>
<td>0.017</td>
</tr>
<tr>
<td>LFa\textsuperscript{b}, ms\textsuperscript{2}</td>
<td>2058±423</td>
<td>885±415</td>
<td>0.021</td>
</tr>
<tr>
<td>LF, nu</td>
<td>47±11</td>
<td>60±14</td>
<td>0.017</td>
</tr>
<tr>
<td>LF/HF, ms\textsuperscript{2}</td>
<td>0.99±0.46</td>
<td>1.76±0.92</td>
<td>0.012</td>
</tr>
</tbody>
</table>

\( ^a \)A value of \( P < 0.05 \) was considered statistically significant.

\( ^b \)Values are the mean ± SD.

\( ^c \)Values are median ± SE.

Abbreviations: HFa, absolute values of high-frequency component; HR, heart rate; LFa, absolute values of low-frequency component; LF/HF, ratio between low- and high-frequency power components; nu, normalized units; RMSSD, square root of the mean squared differences between consecutive RR intervals; SDNN, standard deviation of normal RR intervals.

#### Assessment of endothelial function

There was no significant difference between the MAP-94 and MAP-84 groups in FMD or in baseline brachial artery...
Autonomic Imbalance in Soccer Players

The most significant observation of this study was that even when BP was within a normal range, a lower SBP correlated with better autonomic modulation of the cardiovascular system in soccer players. This finding was not true for FMD, despite the indication that autonomic imbalance precedes endothelial alteration.

We did not find any research in the literature that showed an association between SBP and these parameters in normotensive subjects. In our study, the MAP-94 group had a significantly higher SBP, DBP, LFnu, and LF/HF ratio than did the MAP-84 group. In addition, HFa, LFa, HFnu, and the time-domain SDNN and RMSSD of the MAP-94 group were significantly lower than those of the soccer players in the MAP-84 group. These results indicate that an increase in MAP of 10 mm Hg is accompanied by an increase in cardiac sympathetic modulation and a decrease in parasympathetic modulation.

The decision to form two groups in our study according to SBP was based on the report of Muneta et al.\textsuperscript{21} that the BP in patients with isolated systolic hypertension is susceptible to fluctuations in modulation of the autonomic nervous system (ANS). These results were confirmed by Lucini et al.,\textsuperscript{22} who also found impairments in cardiac autonomic regulation when comparing subjects with the mean SBPs of 103 mm Hg, 133 mm Hg, and 163 mm Hg. According to Lucini and colleagues, higher BPs correlate with larger detriments in autonomic control of the heart, seen by spectral analysis. They found increases in LFnu, LFa, HFa, and the LF/HF ratio, and a reduction in HFnu in their subjects. These results were confirmed in our study, indicating a proportional increase in sympathetic modulation of the cardiovascular system in both in hypertensive patients and healthy subjects.

Indeed, it is very well documented in the literature that the aging process contributes to increased BP.\textsuperscript{23} Buchheit et al.,\textsuperscript{24} examining soccer players who were 13, 15, and 17 years old, showed that even in young athletes, it was possible to identify variations in BP control associated with these athletes’ biological maturation. On the other hand, little is known about the changes that may occur in BP control when MAP is within a normal range.\textsuperscript{24} This uncertainty indicates that it is still a challenge to understand the mechanisms that may be involved in

### Table 2. Brachial artery characteristics of athletes in supine position

<table>
<thead>
<tr>
<th></th>
<th>MAP-84 (n = 15)</th>
<th>MAP-94 (n = 14)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-DIA, mm</td>
<td>0.331 ± 0.041</td>
<td>0.348 ± 0.045</td>
<td>0.305</td>
</tr>
<tr>
<td>RH-DIA, mm</td>
<td>0.363 ± 0.048</td>
<td>0.388 ± 0.042</td>
<td>0.147</td>
</tr>
<tr>
<td>FMD, %</td>
<td>9.438 ± 3.788</td>
<td>11.835 ± 5.627</td>
<td>0.187</td>
</tr>
<tr>
<td>Before NTG, mm</td>
<td>0.336 ± 0.045</td>
<td>0.352 ± 0.047</td>
<td>0.357</td>
</tr>
<tr>
<td>After NTG, mm</td>
<td>0.387 ± 0.040</td>
<td>0.414 ± 0.047</td>
<td>0.100</td>
</tr>
<tr>
<td>NTG, %</td>
<td>15.680 ± 6.171</td>
<td>18.523 ± 7.903</td>
<td>0.335</td>
</tr>
</tbody>
</table>

Abbreviations: B-DIA, basal brachial artery diameter; FMD, flow-mediated dilation; NTG, brachial artery diameter with nitroglycerin; RH-DIA, brachial artery diameter with reactive hyperemia

Values are the mean ± SD.

*A value of $P < 0.05$ was considered statistically significant.

Figure 1. Ratio of low- to high-frequency power components (LF/HF), reflecting autonomic balance in the MAP-84 and MAP-94 groups. *$P < 0.005$. 

BP in patients with isolated systolic hypertension is susceptible to fluctuations in modulation of the autonomic nervous system (ANS). These results were confirmed by Lucini et al.,\textsuperscript{22} who also found impairments in cardiac autonomic regulation when comparing subjects with the mean SBPs of 103 mm Hg, 133 mm Hg, and 163 mm Hg. According to Lucini and colleagues, higher BPs correlate with larger detriments in autonomic control of the heart, seen by spectral analysis. They found increases in LFnu, LFa, HFa, and the LF/HF ratio, and a reduction in HFnu in their subjects. These results were confirmed in our study, indicating a proportional increase in sympathetic modulation of the cardiovascular system in both in hypertensive patients and healthy subjects.

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the physiopathology of essential hypertension or in the initiation of idiopathic pulmonary arterial hypertension.

In our study, although the VO\textsubscript{2\text{max}} indicated that the physical fitness level of the two groups of athletes in the study was very similar, their BP was nevertheless significantly different, and the median BP was used as a cutoff point to obtain the two groups. Indeed, Shehab and Abdulle,\textsuperscript{25} while studying cognition and autonomic function in normotensive subjects, found that lower values of SBP and DBP were inversely related to significantly higher values of SDNN and RMSSD. These results are in agreement with ours, which also showed an inverse relation between BP and SDNN and RMSSD. It is clear in the literature that impaired HRV induces an increase in BP or vice versa. La Rovere et al., studying patients of both sexes with a recent myocardial infarction,\textsuperscript{26} demonstrated that an SDNN below 70 ms was associated with a higher risk for cardiovascular mortality in 1,071 subjects analyzed prospectively for autonomic tone and reflexes after myocardial infarction, and showed the relevance of SDNN for better understanding how modulation by the ANS can decrease the risk of cardiovascular disease.

We also found that RMSSD, SDNN, HF\textsubscript{a}, HF\textsubscript{nu}, LF\textsubscript{nu}, and the LF/HF ratio were impaired in the MAP-94 group in our study as compared with the MAP-84 group, but found no difference in FMD in the two groups. These results indicate that when MAP is increased by 10 mm Hg, autonomic control of the heart worsens without endothelial alteration. We did expect a lower FMD in the MAP-94 group. The inverse relationship between sympathetic tone and endothelial function\textsuperscript{11,16} and the ability of the parasympathetic nervous system to modulate inflammatory responses\textsuperscript{27} indicate that there is a strong association between the ANS and endothelial function. On the other hand, the MAP-94 group in our study did not show either a difference from the MAP-84 group in FMD or an association between the ANS and FMD.

This hypothesis might be complicated by the finding by Lazdam et al,\textsuperscript{17} of an association between endothelial function and cardiovascular phenotype in their study of endothelial function in healthy young people. Their findings indicate an inverse association between BP and endothelial response. In contrast, our results indicate that autonomic imbalance might precede an alteration in endothelial function. The timing of the analysis of ANS modulation in our study and that of Lazdam et al., and the basing of our results on healthy young people who were exercising, could explain the difference in the two studies’ findings.

Moreover, we also found an inverse correlation between SBP and SDNN, the latter of which is a measurement representative of HRV. Similar results were obtained by Erden et al.,\textsuperscript{28} who found an inverse correlation between SBP and SDNN when evaluating the association between nocturnal BP and cardiac autonomic function in untreated hypertensive and normotensive subjects.

On the other hand, although our study makes important contributions to the understanding of mechanisms involved in the regulation of BP, it has limitations. In the study, BP was measured only once, without considering the circadian variation in BP, and VO\textsubscript{2\text{max}} was measured indirectly. Nevertheless, our findings indicate that in young soccer players, an increase in MAP of 10 mm Hg, even within an optimal range of BP, produces a difference in autonomic modulation regardless of endothelial function and VO\textsubscript{2\text{max}}. In accordance with this observation, it is reasonable to believe that under the conditions in our study, the difference in autonomic modulation observed in the MAP-94 group was not accompanied by a change in endothelial function. However, further studies are needed to confirm this hypothesis.

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DISCLOSURE

The authors declare that they have no conflicts of interest.

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