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Epidemiology

Measures of Total Stress-Induced Blood Pressure Responses Are Associated With Vascular Damage

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Background: The role of cardiovascular reactivity to study hypertension, and the assessment methods, are still controversial. We aimed to verify the association of hypertension and vascular damage with several measures of cardiovascular response.

Methods: We studied 40 patients with normal-high (132 ± 1/87 ± 1 mm Hg) blood pressure (Group 1) and 80 untreated hypertensive subjects. Postischemic forearm vascular resistance (mFVR) served to differentiate hypertensive subjects (142 ± 2/92 ± 1 mm Hg *v* 143 ± 2/94 ± 2 mm Hg, P = NS) with a lower (Group 2) and higher (Group 3) hemodynamic index of vascular damage (4.8 ± .05 *v* 6.3 ± .09, $P < .001$). Reactivity was induced by Stroop (5') and cold pressor (90") tests. We measured muscular contraction and skin conductance as indices of emotional arousal, blood pressure, heart rate, forearm blood flow, and vascular resistance. Reactivity measures included: a) change from baseline, b) residualized score, c) cumulative change from baseline and residualized score, and d) total reactivity as area-under-the-curve (AUC), including changes occurring during baseline and recovery phases.

Results: The AUC of systolic blood pressure, diastolic blood pressure, and mFVR progressively increased in the groups ($P < .001$). Corrections of anthropometric and metabolic confounders were introduced in the Pearson equation between mFVR and reactivity measures. The AUC of SBP, DBP, and forearm blood flow and resistance demonstrated the highest ($P < .001$) correlation. On multiple regression analysis, AUC of SBP ($\beta = 0.634$) and forearm blood flow ($\beta = -0.337$) were predictive ($P < .001$) of vascular damage.

Conclusions: Total blood pressure stress response, as AUC, including baseline and recovery phases, was significantly better associated with hypertension and vascular damage than the other reactivity measures studied. Am J Hypertens 2005;18:1226–1232 © 2005 American Journal of Hypertension, Ltd.

Key Words: Cardiovascular reactivity, hypertension, vascular damage.

Exaggerated cardiovascular reactivity to behavioral challenges has been suggested as a potential factor enhancing the risk of hypertension and coronary artery disease.[1] Furthermore, increased diurnal blood pressure (BP) variability, which is related to target organ damage, has been attributed mainly to psychological stressors.[2,3]

A number of different methods have been used to study the relationship between cardiovascular diseases and hypertension. Ambulatory BP monitoring techniques, although suitable for clinical purposes, do not permit the study of cardiovascular reactivity in standardized conditions. On the contrary, laboratory challenges may be applied in controlled environments while multiple biological and hemodynamic variables are being monitored.

Studies adopting different laboratory techniques to monitor cardiovascular functions have provided convincing evidence of the causal effects of behavioral factors as triggers of myocardial ischemia.[1] On the other hand, the evidence supporting a relationship between exaggerated cardiovascular responses and hypertension is still controversial.[4,5] This might be ascribed mainly to the nature of the stressors, the individual emotional activation, and the measure of cardiovascular reactivity.[6] Until now, very few

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studies have used extracardiovascular neuroautonomic variables to verify the degree of emotional participation in the stressors presented.[7,8] Moreover, although a failure to recover baseline values has been reported in patients with a risk of hypertension, most studies have not considered recovery as a potential measure of cardiovascular reactivity.[9]

The aim of the present study was to demonstrate which measure of cardiovascular response to laboratory stressors—absolute, residualized, aggregate or total—conducted in a controlled environment and evaluating individual emotional activation, might be best associated with the hypertensive state and the progression of vascular damage.

Methods

At the Hypertension Unit of our institution we enrolled 40 consecutive subjects (Group 1) with normal-high BP (132 ± 1/87 ± 1 mm Hg) and 80 consecutive subjects with untreated grade 1 hypertension (143 ± 2/93 ± 1 mm Hg). In accordance with our day-hospital protocol for primary diagnosis or control of hypertension, the subjects underwent physical examinations, electrocardiography, chest x-rays, and fasting blood chemistry tests to exclude secondary hypertension. The stress session was authorized by the Hospital Direction. The procedures were performed in accordance with the Institutional Review Board. Patients with a positive history of cerebral, coronary, or peripheral vascular diseases were excluded. Informed consent was obtained from all patients.

Laboratory Methods

The study featured an open design consisting firstly of a 4-week controlled run-in period, during which no treatment for hypertension or metabolic disorders was administered.

To avoid anxiety about a new medical examination, patients were invited to visit the laboratory first and to become familiar with the equipment. On the day of the test, patients arrived in the laboratory after a 12-h fasting period. After 10' of rest in supine position the heart rate and BP were measured in triplicate in both arms and the measures were averaged. The cardiovascular reactivity study was performed between 9:00 and 10:30 AM, after 20' of acclimatization, in a quiet temperature-controlled room (22°C), with patients in supine position. We adopted the following mental and physical tasks. The Color Word Stroop test, 5' long, based on incongruent visual input, consisted of asking the patients to recognize, within a time limit, in what colored ink the name of an incongruous color word was printed. The cold pressor test, 90" long, consisted of immersion of the right foot, up to the ankle, into iced water (4°C). Each task was preceded and followed by 10'-long observation phases (baseline 1; interposed recovery–baseline 2; final recovery).

Different neurovegetative and hemodynamic variables were continuously taken noninvasively and the values were averaged every minute. The muscular contraction level (μV), related to alertness, was monitored at the forehead with two surface electrodes and a third neutral electrode in between. The skin conductance level (microsiemens [μS]), an index of emotional arousal,[7] was recorded using electrodes taped to the palmar surfaces of the fourth and fifth finger of the left hand. The above measures were taken to confirm the emotional impact of the laboratory stimuli. Systolic BP (SBP), mean BP (MBP), diastolic BP (DBP) (all in mm Hg), and heart rate (HR; beats/min) were continuously monitored using the Ohmeda 2300 Finapres (Ohmeda Monitoring System, Englewood, CO) at the middle finger mid-phalanx of the left hand. The equipment had output to a personal computer for on-line computation. Forearm blood flow (FBF; mL/min/100 g) and forearm vascular resistance (FVR; MBP/FBF, Ua) were measured by venous occlusion plethysmography (D.E. Hokanson Inc. EC-5R+E-10, Issaqua, WA) by a method previously described.[10] Briefly, a mercury-in-sylastic strain-gauge was placed 5 cm below the antecubital crease of the right forearm, supported above the level of the heart, at a 30-degree angle to the horizontal. To arrest the hand circulation, a pediatric arterial occlusion cuff was placed around the wrist and inflated at 200 mm Hg for 1' before any measurements. Forearm vascular measurements were started at min 1, 5, and 9 of each of the baseline and resting/recovery phases, at min 2 and 4 during mental stress and at sec 30 during physical stress. After 10' of rest, we measured postischemic blood flow (MFBF). Postischemic hyperemia, which elicits endothelium-dependent vasodilation, served as an index of the vasodilatory capacity and the residual (minimal) vascular resistance (mFVR: MBP/MFBF, Ua) was used as a hemodynamic index of vascular damage.[11] Both MFBF and mFVR were determined from the measurements obtained during the 30" to 60" after forearm ischemia. This was induced by inflating the upper cuff to 200 mm Hg for 10' and superimposing a 5"-handgrip exercise, every 30," during the first 9 min.[10,11]

To evaluate stress reactivity in hypertensive patients with grade 1 hypertension with different vascular damage, these patients were divided into two groups: 40 with lower (Group 2) and 40 with higher (Group 3) values of mFVR.

Reactivity Measures

To calculate reactivity to a single stressor, baseline values were considered as the average of measures obtained during the last 3 min of the first phase (baseline 1) and the second 10' (interposed recovery–baseline 2) phase.

The study was based on assessment, for each stressor, of the change from baseline (first and second), calculated as the difference between averaged measurements during the task and the relative baseline value.[12] Residualized change scores for each task were also computed to avoid the impact of baseline on reactivity measure.[13] As responses to both stressors, cumulative change from baseline and cumulative re-

sidualized scores were calculated as the sum of differences between tasks and averaged baselines.[13,14]

Cardiovascular reactivity in hypertensive subjects is frequently characterized by a prolonged response time.[4,9] Thus, total stress reactivity, including the mental and physical tasks as well as the baseline and recovery phases, was calculated as area-under-the-curve (AUC) = (value · time). The AUC improves the one-dimensional time-to-recovery measure, because it controls for the steepness of decline in the level of the physiologic parameter.[14]

Data were analyzed with the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL). Post hoc analysis by the Student-Newman-Keuls test was used to compare groups. A two-tailed P value $< .05$ was considered statistically significant. The Pearson test and stepwise multiple regression analysis were applied to analyze the association of vascular damage with office values and reactivity measures. Values are shown as mean ± standard error of the mean in the text and tables and as the mean ± standard deviation in the figures.

Results

The cardiovascular reactivity study did not need to be suspended in any patient but three patients underwent blood chemistry tests again on the following day because of laboratory accidents.

According to the study design, SBP and DBP office values were significantly lower in Group 1 than in the other two groups. HR office values were similar (Table 1). Sex distribution, a positive family history of hypertension, smoking habit, and BMI were similar among patients. Estimated history of hypertension and age were lower in Group 1 (Table 1). Blood glucose was slightly lower in Group 2 but total and LDL-cholesterol were higher in Group 2 than in Group 1. In Group 3 total and HDL cholesterol were lower than Group 1 and 2. Triglycerides were similar in all the groups (Table 1). Vasodilatory capacity presented progressively decreased values in Groups 2 and 3 and, inversely, mFVR was significantly and progressively higher in these two groups (Table 1).

Muscular contraction and skin conductance baseline

Table 1. Patients classified by hypertensive state, hemodynamic index of vascular damage, and their total reactivity

Characteristic	Normotensive patients with normal-high blood pressure (group 1)	Hypertensive patients with lower (mFVR) vascular damage (group 2)	Hypertensive patients with higher (mFVR) vascular damage (group 3)
Office value			
SBP (mm Hg)	131 ± 1	143 ± 2***	144 ± 2***
DBP (mm Hg)	88 ± 1	93 ± 1***	94 ± 2***
Heart rate (beats/min)	78 ± 2	77 ± 2	77 ± 2
Characteristic			
Sex (male/female)	29/11	21/19	27/13
Age (y)	42 ± 1	46 ± 2*	45 ± 1
Family history of hypertension	32	35	35
History of hypertension (mo)	22 ± 4	35 ± 6*	33 ± 5*
Smoke (cigarettes/day)	10 ± 2	11 ± 2	11 ± 1
Body mass index (kg/m^2)	28.30 ± 0.58	29.49 ± 0.63	28.79 ± 0.55
Blood glucose (mg/dL)	93 ± 3	85 ± 2**	88 ± 2
Total cholesterol (mg/dL)	221 ± 6	240 ± 6*	218 ± 6††
LDL cholesterol (mg/dL)	138 ± 5	154 ± 5*	141 ± 5
HDL cholesterol (mg/dL)	53 ± 2	58 ± 2	51 ± 2†
Triglycerides (mg/dL)	149 ± 12	140 ± 8	131 ± 8
Vascular property			
MFBF (mL/min/100 gr)	27.49 ± 0.60	22.43 ± 0.46***	17.98 ± 0.44***,†††
mFVR (Ua)	3.76 ± 0.07	4.94 ± 0.06***	6.28 ± 0.09***,†††
Total reactivity as AUC			
SBP	4916 ± 71	5340 ± 76***	5765 ± 77***,†††
DBP	2771 ± 41	3004 ± 31***	3197 ± 40***,†††
HR	2800 ± 61	2778 ± 64	2821 ± 48***
FBF	159 ± 7	137 ± 6*	121 ± 4***,††
FVR	1010 ± 36	1199 ± 54**	1311 ± 54***

AUC = area under the curve; DBP = diastolic blood pressure; FBF = forearm blood flow; HR = heart rate; MFBF = maximal (postischemic) forearm blood flow; mFVR = minimal (residual) forearm vascular resistance; SBP = systolic blood pressure.

(* $p < 0.05$, ** $p < .01$, *** $p < .001$ vs normotensive subjects with normal-high blood pressure. † $P < 0.05$, †† $P < 0.01$, ††† $P < 0.001$ vs hypertensives with lower vascular damage).

values were similar in the three groups. Muscular contraction absolute change and residualized scores were comparable among patients. Skin conductance change from baseline during mental stress was lower in Group 3. Residualized scores to both stressors were similar. The aggregate measures of reactivity, expressed as cumulative change from baseline, cumulative residualized score, and AUC were similar in the three groups and confirmed an equivalent alertness and emotional arousal.

As expected, Group 1 showed significantly ($P < .001$) lower baseline values of SBP/DBP (126 ± 2/82 ± 1) than Group 2 (137 ± 2/90 ± 1) and Group 3 (138 ± 2/91 ± 2). However, HR (73 ± 1 *v* 71 ± 2 *v* 72 ± 2, respectively) and FBF (3.96 ± 0.2 *v* 3.63 ± 0.19 *v* 3.51 ± 0.17, respectively) were similar among groups. On the contrary, FVR at baseline was higher in hypertensive subjects with lower mFVR (31.88 ± 1.71, $P < .05$) and higher mFVR (31.96 ± 1.68, $P < .001$) than in patients with normal-high BP (26.86 ± 1.18).

During mental stress, hypertensive subjects were characterized by an increased change from baseline with regard to SBP, but for HR this was significantly higher only in Group 3. Values for DBP, FBF, and FVR were similar in all three groups. During the cold pressor test the change from baseline for DBP was the least marked in Group 2 but Group 3 also showed enhanced HR reactivity (Fig. 1).

The residualized scores for SBP and DBP during mental stress were significantly and progressively higher in Groups 2 and 3 but HR and FVR were higher only in Group 3. The FBF showed similar responses. During the cold pressor test, the residualized score was higher for SBP in both groups of hypertensive subjects, whereas for DBP it was higher only in Group 3. Residualized scores were similar for the other hemodynamic variables (Fig. 1).

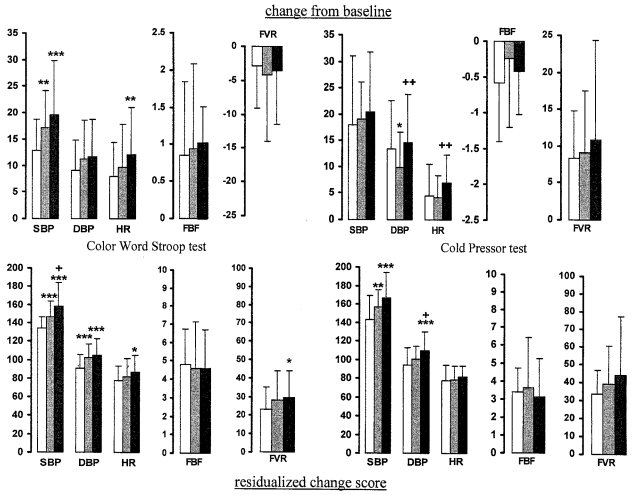

FIG. 1 Hemodynamic reactivity to a single stress as change from baseline and residualized change score. DBP = diastolic blood pressure; FBF = forearm blood flow; FVR = forearm vascular resistance; HR = heart rate; SBP = systolic blood pressure. **Open (white) bars** indicate Group 1 (normotensive subjects with normal-high blood pressure); **shaded (gray) bars,** Group 2 (hypertensive subjects with lower hemodynamic index of vascular damage); **filled (black) bars,** Group 3 (hypertensive subjects with higher hemodynamic index of vascular damage). $*P < .05$, $**P < .01$, $***P < .001$ *v* normotensive subjects with normal-high blood pressure. $+P < .05$, $++P < .01$, $+++<P < .001$ *v* hypertensive subjects with lower hemodynamic index of vascular damage).

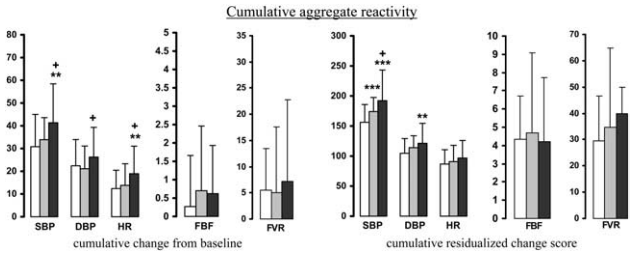

FIG. 2 Hemodynamic aggregate reactivity to both stressors as cumulative change from baseline and cumulative residualized change score. **Open (white) bars** indicate Group 1 (normotensive subjects with normal-high blood pressure); **shaded (gray) bars,** Group 2 (hypertensive subjects with lower hemodynamic index of vascular damage); **filled (black) bars,** Group 3 (hypertensive subjects with higher hemodynamic index of vascular damage). $*P < .05$, $**P < .01$, $*** P < .001$ *v* normotensive subjects with normal-high blood pressure. $+P < .05$, $++P < .01$, $+++<P < .001$ *v* hypertensive subjects with lower hemodynamic index of vascular damage). Abbreviations as in Fig. 1.

Cumulative change from baseline was higher for SBP, DBP, and HR for hypertensive subjects with higher mFVR (Group 3) (Fig. 2). The cumulative residualized score was significantly and progressively higher for SBP in Groups 2 and 3 but for DBP it was higher only in the Group 3 (Fig. 2).

Total stress reactivity (expressed as AUC) including baseline, test, and recovery phases demonstrated a very high, significant, and progressively greater SBP and DBP response in Groups 2 and 3 but no difference for HR. The FBF total reactivity showed a significant and progressive reduction in Groups 2 and 3, whereas both groups demonstrated a significant increase of FVR total response (Table 1).

Pearson partial correlations were computed to highlight the association between mFVR and different measures of reactivity. Office BP and HR values, age, estimated history of hypertension, BMI, blood glucose, and lipids were introduced in the equation to control for possible confounders. Absolute change from baseline was related to mFVR only for SBP during mental stress and for HR during physical stress (Table 2). The residualized score was associated only for SBP during both stressors whereas FBF was negatively correlated during the cold pressor test (Table 2). Cumulative change from baseline was associated with mFVR for SBP and HR but cumulative residualized score was related to vascular damage only for SBP (Table 2). The AUC was significantly associated with mFVR for SBP, DBP, and FVR and negatively correlated for FBF (Fig. 3).

Stepwise multiple regression analysis with mFVR as the dependent variable and the hemodynamic measures as independent variables showed that among the office values, only SBP ($\beta = 0.378$, $P < .001$), and not DBP ($\beta = -0.247$, P = NS) or HR ($\beta = -0.128$, P = NS), was

Table 2. Pearson correlations between cardiovascular reactivity measures and hemodynamic index of vascular damage (mFVR)

	Color Word Stroop test, change from baseline 1	Cold pressor test, change from baseline 2	Color Word Stroop test, residualized score	Cold pressor test, residualized score	Cumulative (both stressors), change from change	Cumulative (both stressors), residualized score
SBP	0.193*	0.047	0.238†	0.202*	0.204*	0.311†
DBP	0.051	0.135	0.095	0.173	0.130	0.121
HR	0.148	0.219*	0.146	0.085	0.206*	0.084
FBF	0.102	−0.029	−0.064	−0.241*	0.075	0.083
FVR	0.033	0.106	0.041	0.154	0.105	0.125

Abbreviations as in Table 1.
* $P < .05$; † $P < .01$.

significantly associated with mFVR. Among measures of reactivity to a singular stressor, only residualized scores for SBP to the mental ($\beta = 0.579$, $P < .001$) and FBF to the physical test ($\beta = -0.343$, $P < .001$) entered into the equation. When the aggregate measures (cumulative and total) of stress response were considered, only SBP ($\beta = 0.605$, $P < .001$), FBF ($\beta = -0.511$, $P < .001$), and FVR ($\beta = 0.247$, $P < .05$) total reactivity entered into the equation. Again, when the reactivity measures were considered all together, SBP ($\beta = 0.634$, $P < .001$) AUC, at the first step, and FBF ($\beta = -0.337$, $P < .001$) AUC, at the second step, entered into the equation, showing high significance.

Discussion

The findings suggest that the AUC, as a measure of total cardiovascular reactivity including the ability to recover the baseline value, is significantly predictive of vasoconstrictive damage and associated with reduced functional peripheral blood flow. As previously defined,[13] "cardiovascular reactivity might be considered part of the inter-individual hemodynamic variability observed during a laboratory task. . . ." For this reason, different protocols and numerous measures were used to identify hemodynamic responses predictive of cardiovascular disease. Although some studies showed that as a prognostic indicator of hypertension, cardiovascular reactivity is poor or ineffective,[5,9,12] other findings suggest that response to laboratory stressors might be predictive of established office[15] and ambulatory[16] hypertension. The evidence that cardiovascular reactivity was found associated, even after multivariate risk-factor adjustment, to impaired vasodilation and to the onset of vascular[3,10] and left ventricular[17] changes, encourages further studies on the clinical use of laboratory hemodynamic reactivity.[18]

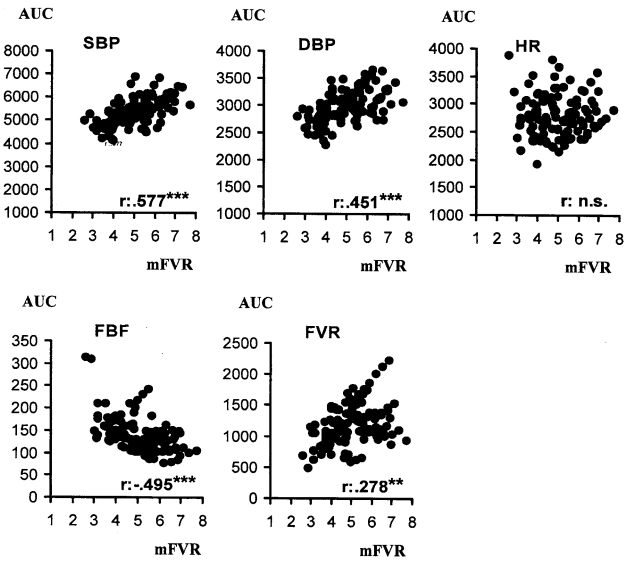

FIG. 3 Pearson tests between total reactivity, indicated as total response as area under the curve (AUC) of the different hemodynamic variables and hemodynamic index of vascular damage, indicated as minimal forearm vascular resistance as hemodynamic index of vascular damage (mFVR). Abbreviations as in Fig. 1.

The hemodynamic response to mental stimuli, consisting of the combination of a reduction in blood supply and an increase in cardiac demand, might explain the role of mental stress in the onset of myocardial ischemia[1] and in the rise of cardiovascular damage in hypertensive individuals.[19] Moreover, peripheral alterations may increase reactivity in individuals with normal emotional neuroendocrine responses.[20] Our hypertensive subjects, in fact, had no significant differences with regard to familial history and estimated duration of hypertension, BMI, and smoking habit; but those with the highest mFVR value, which is associated with microvascular angina,[21] showed the highest BP reactivity.

It has been demonstrated[14,22,23] that to increase the number of measures and to expand the time of investigation, the use of aggregate responses to different tasks may be the best psychometric methodology for achieving more reliable computation of cardiovascular response. Therefore we extended measurements throughout the session and we adopted extracardiovascular variables, namely muscular contraction and skin conductance, to verify differences in emotional arousal.

With the adoption of these procedures, our findings confirm that mental stressors may elicit greater BP vari-

ability in hypertensive individuals.[1,16] Moreover, the findings demonstrated that the residualized score, in terms of both single and aggregate BP response, represents a more reliable reactivity measure than absolute changes, probably because it is able to prevent the impact of the baseline value on the calculated change.[12] In fact, residualized and cumulative residualized scores characterize hypertensive subjects and tend to discriminate those with greater vascular damage. In contrast, the AUC was used to assess reactivity from baseline and to control the acceleration, peak, and duration of the individual stress response and the ability to recover baseline values. As suggested, "although the response may be influenced by the initial baseline value, the problem may be resolved by considering the recovery phase as part of the same task protocol and by calculating a single AUC that covers the entire time span, from baseline to the last measurement."[14] The method has also been applied to investigate changes in hemodynamic reactivity induced by medications[10] as well as to analyze consecutive biomedical samples.[24]

When SBP and DBP responses were calculated as AUC, reactivity significantly and progressively increased in Groups 2 and 3. Patients in these groups were also characterized by reduced vasodilation and increased vasoconstriction secondary to arterial thickening.[20] The findings suggest that the sensitivity of the reactivity measure in distinguishing the hypertensive state is improved when the recovery phase is included in the calculation. As previously suggested, once structural remodeling of resistance vessels has begun and vascular wall thickening increases, hemodynamic responses to any stimulus raising BP will lead to an exaggerated or protracted pressure/flow dynamic response.[25] Thus the carryover measure AUC, more than other measures, might detect important prognostic consequences besides those offered by the response to a laboratory task.[8,14]

Although the stability and predictivity[3,16,26] of hemodynamic stress responses in hypertensive subjects have been demonstrated, the application of cardiovascular reactivity as a potential clinical approach is still controversial.[5,27] Our results suggest that this may be ascribed mainly to the omission of recovery from the reactivity computation. In fact, patients may differ with regard to emotional participation in a presented stressor, peak response, and ability to recover the baseline value of the hemodynamic function. All of these characteristics, which are mutually related, should be considered when cardiovascular reactivity is studied. The measure of the AUC includes all these attributes in one measure only and considers cardiovascular reactivity as a dynamic biological response.[14,24]

The study of laboratory cardiovascular reactivity in patients at risk for hypertension requires a number of conditions: a primary activation of the central nervous system triggering enhanced sympathetic activity[7,28]; a secondary cardiac and/or vascular response; a consequent BP change; and, finally, a method of computation predictive of hemodynamic alteration and the onset of target organ damage.[2,10,13,16] We used extracardiovascular functions to confirm central nervous system activation and to demonstrate that differences in hemodynamic responses between groups were not secondary to different emotional arousal. We used the total measure of BP stress response, the AUC, to cover in one single measurement the initial rest, the peak response, and the entire stress-recovery time. Moreover, this measure, compared with the other stress response computations, showed the highest significant association with the index of vascular damage.

We are aware that there are limits to a cross-sectional study of the statistical predictivity of vascular damage. We therefore recognize the need to perform a prospective study to confirm the ability of BP reactivity, expressed as AUC, to highlight the vascular risk in hypertensive subjects.

Patients at risk for hypertension and those with vascular damage[29,30] have demonstrated a reduced vasodilatory capacity, sustained BP response, and failure to recover properly after laboratory stressors. Our findings showed that patients with the greatest BP reactivity in terms of AUC showed the greatest reduction in FBF during stress, the lowest endothelium-dependent vasodilation, and the highest index of vascular damage.

Our method adopts psychometric and biological parameters, considers the multiple baseline–stress-recovery measures, computes the individual response to different stimuli, and includes time as a necessary biologic indicator of the stress response.

The assessment of anticipatory, peak, and recovery measures might lead to a more appropriate model of the stress–disease relationship serving as a marker of preclinical alterations in vascular resistance.[21,23] In fact, although the study cannot demonstrate a causative role of BP reactivity in the onset of hypertension, the total response expressed as AUC may distinguish, better than BP office values, hypertensive subjects with more marked endothelial damage and a consequent prolonged BP stress response.

In conclusion, the AUC represents a reliable and upgraded measurement of cardiovascular reactivity with underlying pathophysiologic links to hypertension. This method may be recommended because it could improve the use of standardized laboratory stress techniques that, possibly combined with ambulatory BP monitoring, may represent a clinical approach helping to differentiate more complicated hypertensive states and increased risk for cardiovascular events.

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