Allostatic overload in patients with essential hypertension

ALLOSTATIC OVERLOAD IN PATIENTS WITH ESSENTIAL HYPERTENSION

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Abstract

The role of psychosocial stress in the development of essential hypertension has attracted increasing attention in the last decades, even though research findings have been often inconclusive. We specifically investigated allostatic overload (AO) in hypertensive patients using a clinimetric approach. Allostatic overload was assessed by a semi-structured research interview based on clinimetric criteria in 80 consecutive outpatients with essential hypertension (46.3% females; mean age 62.18±8.59 years; age range 47-74 years) and 80 normotensive matched controls. Three clinical interviews and two self-rating questionnaires for assessing psychological distress and well-being were also administered. Cardiac variables were collected.AO was present in 26 (32.5%) of the hypertensive patients based on clinical interviewing, and in only 6 normotensive controls (p<.001). Hypertensive patients with AO had significantly higher levels of psychological distress than those without. Further, patients with AO displayed significantly lower levels of well-being and quality of life (p<.001). A significantly greater prevalence of psychosomatic syndromes was found to be associated with the presence of AO (p<.05), whereas no significant association was detected as to psychiatric diagnoses. Significantly greater cardiovascular risk was found among hypertensive patients reporting AO compared to those without (p<.05). The results of this study support the clinical relevance of a psychological assessment of hypertensive patients, with important implications for the non-pharmacological management of hypertension.

Keywords: allostatic overload; hypertension; clinimetrics; psychological distress; stress; Diagnostic Criteria for Psychosomatic Research (DCPR)

AO = allostatic overload, **CID** = Clinical Interview for Depression, **DBP** = diastolic blood pressure, **DCPR** = Diagnostic Criteria for Psychosomatic Research, **DSM-5** = Diagnostic and Statistical Manual of Mental Disorders, fifth edition, **PSI** = PsychoSocial Index, **SBP** = systolic blood pressure, **SCORE** = Systematic COronary Risk Evaluation, **SQ** = Symptom Questionnaire

1. Introduction

The role of psychosocial stress in the development of essential hypertension has attracted increasing attention in the last decades, but it is still a source of considerable controversy. Research findings have been often inconclusive, and large heterogeneity exists among studies as to the definition of stress and methodological quality (Sparrenberger et al., 2009; Spruill, 2010; Mann, 2012; Cuffee et al., 2014; Cuevas et al., 2017; Liu et al., 2017; Mocayar Maròn et al., 2019). Since hypertension remains the major preventable cause of cardiovascular disease and evidence demonstrates that lowering blood pressure can substantially reduce premature morbidity and mortality (Williams et al., 2018), the role of psychosocial stress in the development and progression of hypertension demands special consideration.

Several psychosocial factors (occupational stress, low socio-economic status, racial discrimination, marital stress, social isolation, negative emotional states) have been found to be associated with higher circulating levels of catecholamines, higher cortisol levels, exaggerated cardiovascular response, increased blood pressure over time, and greater risk for the onset of hypertension (Everson-Rose and Lewis, 2005; Sparrenberger et al., 2009; Spruill, 2010; Cuffee et al., 2014; Cuevas et al., 2017; Liu et al., 2017; Gillespie et al. 2019). Maladaptive behavioral responses (such as poor adherence to treatment, obesity, physical inactivity, alcohol consumption and smoking) do also account, to a considerable extent, for the association between psychosocial stress and hypertension (McCubbin et al., 2018; Williams et al., 2018).

The concept of allostatic load (McEwen and Stellar, 1993; McEwen, 2008; Fava et al., 2019) reflects the cumulative effects of experiences in daily life that involve ordinary events (subtle and long-standing life situations) as well as major challenges (life events), and also includes the physiological consequences of the resulting health damaging-behaviors, including poor sleep, lack of exercise and poor diet. These aspects were often overlooked in conventional thinking about "stress".

A considerable number of studies have attempted to identify allostatic load by use of laboratory biological markers and physical parameters (McEwen, 2008; McEwen and Wingfield, 2010; McEwen, 2017; Fava et al., 2019). Biological parameters of allostatic load have been linked to decline in physical functioning and mortality (Buckwalter et al. 2016). However, they express a state of the body systems, but are nonspecific mediators and do not provide information on the underlying individual experiential causes. To fill this gap and improve patient assessment, clinimetric criteria for the determination of allostatic overload based on clinical grounds have been developed (Fava et al., 2010, 2017, 2019). The clinimetric evaluation of allostatic overload has some major advantages compared to other classic stress-related models and may help identify individuals that are clinically stressed, based on specification of the stressor and both the

physiological and cognitive components of the stress response (Fava et al. 2019). The clinimetric criteria have been applied in several studies to patients with cardiovascular disease (Porcelli et al., 2012; Offidani et al., 2013; Gostoli et al., 2016; Guidi et al., 2016). Among outpatients with essential hypertension and coronary heart disease (Porcelli et al., 2012), allostatic overload was found to be related to poorer psychosocial functioning, higher rates of psychopathology, and a higher disease-related emotional burden.

The aim of this study was to determine the prevalence of allostatic overload, based on clinimetric criteria, among hypertensive outpatients compared to normotensive control subjects, and to comprehensively assess the associated psychological features (both by clinical interview and self-rating scales) and health variables. We hypothesized to find a higher prevalence of allostatic overload in hypertensive patients compared to normotensive controls. Within the hypertensive population, we expected to find higher levels of psychological distress, impaired psychological well-being, and increased cardiovascular risk in patients with allostatic overload than in those without.

2. Methods

2.1 Participants and Procedures

Eighty outpatients (43 men, 53.8%, and 37 women, 46.3%; mean age 62.18±8.59 years; age range 47-74 years) affected by essential hypertension, referred by the general practitioner for standard control visits at the outpatients' Clinic for Cardiovascular Prevention and Hypertension at the Division of Cardiology (Bellaria Hospital, Bologna), were consecutively enrolled in the study between May 2015 and October 2016. Patients were usually referred to a specialized treatment unit for the evaluation of the absolute cardiovascular risk, as part of a secondary prevention program in order to search for or closely monitor target organ damage or cardiac related disease. All patients were on antihypertensive medication at the time of referral to the clinic (i.e., angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists, calcium channel blockers, β-blocking agents, α-blockers, and diuretics). In case of failure to achieve blood pressure control, additional drugs or changes in current treatment strategy were subsequently prescribed. Patients were excluded if they were < 18 or > 75 years old, had cognitive impairments, did not give written informed consent or had psychotic symptoms.

Eighty normotensive control subjects, with no major illnesses and matched for gender and age (46.3% females; mean age 61.09±8.33 years; age range 42-74 years), were recruited from primary care settings during the study period. Sociodemographic and clinical characteristics of both hypertensive patients and matched controls are depicted in Table 1.

Participants underwent a comprehensive psychological evaluation at enrollment by a clinical psychologist with expertise in the field of psychosomatic assessment. Data on cardiac variables were collected from medical records. Written informed consent was obtained from all participants, after the procedures were fully explained to them. The study was approved by the appropriate institutional review boards.

2.2 Assessment

2.2.1 Psychosocial variables

Psychological assessment included both interview-based and self-rating instruments:

a) the semi-structured research interview for assessing allostatic overload (Fava et al., 2019) according to clinimetric criteria (Table 2) (Fava et al., 2010, 2017). Determination of the presence of allostatic overload is performed through clinical interviewing, based on specification of the stressor, psychopathological symptoms, social-occupational functioning and well-being. The interview requires careful exploration of the patient's life circumstances and may help formulate a global clinical judgment of an individual's assets and coping skills in dealing with own current life situation.

b) an adapted version of the Structured Clinical Interview for DSM-5 Disorders for establishing psychiatric diagnoses (First et al., 2015).

c) the Italian version of the semi-structured interview for the Diagnostic Criteria for Psychosomatic Research (DCPR) (Porcelli and Sonino, 2007). The DCPR encompass various diagnostic rubrics: abnormal illness behavior (disease phobia, thanatophobia, health anxiety, illness denial), somatization syndromes (persistent somatization, functional somatic symptoms secondary to a psychiatric disorder, conversion symptoms, anniversary reactions), irritability (irritable mood, type A behavior), demoralization, and alexithymia. The interview for DCPR consists of 58 items scored in a yes/no response format evaluating the presence of 1 or more of 12 psychosomatic syndromes. The interview has shown excellent inter-rater reliability, construct validity, and predictive validity for psychosocial functioning and treatment outcome (Galeazzi et al., 2004). Diagnoses were established independently for DSM and DCPR.

d) the Clinical Interview for Depression (CID) (Paykel, 1985; Guidi et al., 2011) for rating a wide range of affective symptoms. The CID is an observer-rated dimensional assessment tool, an expanded version of the Hamilton Rating Scale for Depression. The CID covers 36 symptom areas, rated on 7-point scales (only 1 item is rated on 4-point scale and 2 items are rated on 3-point scale), with specification of each anchor point based on severity, frequency and/or quality of symptoms. Two summed scores, the 10-item depression and 4-item anxiety scores (depression score range 10-70; anxiety score range

4-28), as well as a total score for all 36 items (total score range 36-241), can be obtained. The CID has been shown to be a valid and reliable instrument to rate the symptoms of depression comprehensively and is particularly suitable for assessing subclinical symptoms of affective disorders, in view of its capability to measure small changes near the normal end of the spectrum (Guidi et al. 2011).

e) the PsychoSocial Index (PSI) (Sonino and Fava, 1998; Piolanti et al., 2016), a 55-item self-rating scale covering domains such as stress, psychological distress, abnormal illness behavior, well-being and quality of life. It offers a synthesis of previously validated instruments. Some questions of the PSI involve specific responses; most require a yes/no answer; others are rated on a Likert 0-3 scale (from "not at all" to "a great deal"). The final item concerning quality of life has five possible choices (from "excellent" to "awful"). The PSI yields different subscale scores: the stress scale consists of 15 items with yes/no answer (score range 0 to 15); the psychological distress scale includes 15 questions rated on a Likert 0-3 scale (score range 0-45); the abnormal illness behavior scale consists of 3 questions rated on a Likert 0-3 scale (score range 0 to 9); the well-being scale includes 6 items with a yes/no answer and the final item on quality of life rated on a Likert 0-4 scale (score range 0 to 10). The PSI has been used in various clinical populations in different countries and showed high sensitivity, discriminating varying degrees of psychosocial impairment in different populations (Piolanti et al., 2016). The PSI items supplement the information provided by the clinical interview for determining the degree of allostatic overload.

f) Kellner's Symptom Questionnaire (SQ) (Fava et al., 1983; Kellner, 1987), a 92-item self-rating instrument yielding four scales: depression, anxiety, somatization and hostility-irritability. Items require a yes/no or true/false answer. Each scale score may range from 0 to 23, where higher scores indicate greater psychological distress. The SQ has been extensively used in clinical research and was found to be a sensitive instrument to detect change.

All assessment instruments have been validated in the Italian version and extensively used in clinical research. They were selected according to the clinimetric principle of incremental validity, based on which each psychological measure should provide a unique increase in information in order to qualify for inclusion. According to the clinimetric approach, both observer- and self-rated tools were administered.

2.2.2 Arterial blood pressure

Hypertension grading was determined by a cardiologist at the time of the referral to the specialized clinic according to the guidelines for the management of arterial hypertension (Williams et al., 2018). Arterial blood pressure may range from optimal (systolic blood pressure [SBP] <120 mm Hg and diastolic blood pressure [DBP] <80 mm Hg), to normal (SBP

120-129 mm Hg and/or DBP 80-84 mm Hg), to high normal (SBP 130-139 mm Hg and/or DBP 85-89 mm Hg); hypertension is classified as mild (Grade 1: SBP 140–159 mm Hg and/or DBP 90–99 mm Hg), moderate (Grade 2: SBP 160–179 mm Hg and/or DBP 100–109 mm Hg), severe (Grade 3: SBP≥180 mm Hg and/or DBP ≥110 mm Hg), isolated systolic hypertension (SBP ≥140 mm Hg and DBP <90 mm Hg).

Blood pressure was measured by trained nurses at the beginning of the screening process. Cuff size was adjusted after measuring the arm circumference. The procedure was started after the participant had been seated for at least 2 minutes with the cuff on the arm, and the arm resting on a table. Blood pressure was measured automatically three times at 1-minute intervals. The mean of the second and third readings was used in this study.

2.2.3 Absolute cardiovascular risk

The absolute cardiovascular risk evaluates the likelihood that a patient with hypertension will suffer from a cardiovascular event, such as myocardial infarction or death, over the course of the next 10 years. The risk is based on the integrated evaluation of different categories of risk factors calculated according to a prediction model on the basis of: (a) gender, age, smoking habits, levels of systolic and diastolic blood pressure, abdominal obesity, dyslipidemia, C-reactive protein,family history of premature cardiovascular disease; (b) hypertension-mediated organ damage; (c) diabetes mellitus; (d) associated clinical conditions. The risk is divided into four categories (i.e., low, moderate, high and very high) according to the Systematic COronary Risk Evaluation (SCORE) chart (Williams et al., 2018).

3. Data analysis

The data were entered in SPSS for Windows 23 (IBM Corporation, Armonk, NY, USA) and descriptive statistics were calculated. The quality of data collection was monitored regularly to assure accuracy and completeness of data.

Student's t-tests for independent samples and chi-squared tests and were used to compare subgroups as to sociodemographic and clinical variables, prevalence of allostatic overload, as well as psychosomatic and psychiatric diagnoses. Multivariate analyses of variance using the general linear model were performed to test for differences between subgroups (i.e., hypertensive patients *vs* normotensive controls; presence *vs* absence of allostatic overload among hypertensive patients) on dimensional psychological measures (i.e., the CID anxiety, depression and total scales; the PSI

stress, psychological distress, abnormal illness behavior and well-being scales; the SQ anxiety, depression, somatization and hostility/irritability scales), after adjusting for potential confounding factors (i.e., age and gender for comparisons between hypertensive patients and normotensive controls; age, gender and cardiovascular risk for comparisons between presence and absence of allostatic overload in hypertensive patients) in all six models. For comparisons between hypertensive patients with and without allostatic overload, estimates of effect size (partial eta-squared) were calculated for each effect. According to guidelines, values ranging from .01 to .05 are considered small, whereas those from .06 to .13 are medium and those greater than .14 are large. For all tests performed, the significance level was set at 0.05, two tailed. Results were expressed as frequencies (percentages) and means (standard deviations).

4. Results

Compared to normotensive controls, hypertensive patients displayed significantly higher levels of psychological distress and impaired well-being according to dimensional psychological measures (Table 3). Based on clinical interviewing, allostatic overload was present in twenty-six (32.5%) of the hypertensive patients, and in only 6 normotensive control subjects (χ^2_1=15.625, p<.001).

There were no differences between hypertensive patients with and without allostatic overload with regard to sociodemographic variables (Table 4). As to dimensional psychological measures, hypertensive patients with allostatic overload had significantly higher levels of psychological distress than those without, by either observer-rated (CID) or self-rating (PSI and SQ) methods, after adjusting for age, gender and cardiovascular risk (Table 5). In particular, a significant association was found between allostatic overload and affective symptomatology, as indicated by the CID anxiety (p=.01), depression (p<.001) and total (p<.001) scores. Significantly higher scores were also obtained on the PSI distress subscale (p<.001), the SQ anxiety (p<.001), depression (p=.001), and somatization (p<.05) scales by patients reporting allostatic overload compared to those who had none. Further, patients with allostatic overload displayed significantly lower levels of well-being and quality of life, as measured by the PSI well-being scale (p<.001). Estimates of effect size ranged from medium to large (Table 5).

A significantly greater prevalence of DCPR diagnoses was found to be associated with the presence of allostatic overload (χ^2_1=6.515, p=.013): 84.6% (n=22) of hypertensive patients with allostatic overload presented with one or more DCPR syndromes (mainly irritable mood 38,5%, illness denial 27% and alexithymia 19%) compared to 55.6% (n=30) of those

without allostatic overload. No significant association was found between allostatic overload and psychiatric diagnoses (DSM-5) (χ^2_1=.382, p=.616).

As to clinical variables, significantly greater cardiovascular risk was found among hypertensive patients reporting allostatic overload compared to those without (p<.01) (Table 4).

5. Discussion

The results of this study support the clinical relevance of a psychological assessment of patients with essential hypertension, and of allostatic overload in particular.

When comparing hypertensive patients to matched normotensive controls, we found a significantly greater prevalence of allostatic overload in the former group, supporting its role as potential risk factor for the development and progression of hypertension (Mocayar Maròn et al., 2019), in line with the results of previous research on psychosocial stress in hypertension (Sparrenberger et al., 2009; Spruill, 2010; Liu et al., 2017).

In our sample, the presence of allostatic overload among hypertensive patients was found to be associated with significantly higher levels of psychological distress, as detected by either clinical interviewing (CID) or self-rating scales (PSI and SQ). In particular, patients displaying allostatic overload were more likely to report significantly higher levels of depressive and anxiety symptoms, and more somatic complaints compared to those who did not present with allostatic overload. The magnitude of these differences ranged from medium to large, thus supporting the clinical relevance of allostatic overload among patients with hypertension. These findings are in line with those of previous studies carried out in the setting of cardiovascular disease using the same clinimetric assessment methods (Porcelli et al., 2012; Offidani et al., 2013; Gostoli et al., 2016; Guidi et al., 2016).

Further, hypertensive patients with allostatic overload showed impaired levels of self-rated psychological well-being and quality of life. A protective role of positive psychological well-being in relation to blood pressure, cardiovascular function and health behaviors has been suggested (Boehm and Kubsanzky, 2012; Trudel-Fitzgerald et al., 2014, 2015; Kubzansky et al., 2018). Indeed, psychological well-being play a buffering role in coping with stress and may have a favorable impact on cardiovascular health (Ryff et al., 2006; Ryff, 2014).

A significantly greater prevalence of DCPR diagnoses was found to be associated with allostatic overload in our sample of hypertensive patients. In particular, the most frequently reported diagnostic rubrics were irritable mood, illness denial and alexithymia. Anger and hostility have been shown to be associated with increased risk of hypertension, even though the cognitive, affective and behavioral dimensions of anger may affect blood pressure differently (Hosseini et al., 2011; Trudel-Fitzgerald et al., 2015; Tilov et al., 2016). Illness denial represents a manifestation of abnormal illness behavior and may hinder the prevention and treatment of medical disorders (Fava et al., 2017). Lack of adherence to treatment (i.e., early discontinuation or suboptimal daily use of treatment) and failure over time of lifestyle modifications (salt restriction, moderation of alcohol consumption, dietary changes, weight reduction, regular physical activity, smoking cessation) are the most important causes of poor control of blood pressure and pseudo-resistant hypertension, and might be associated with specific psychological characteristics (McCubbin et al., 2018; Petit et al., 2018; Williams et al., 2018). Alexithymia has been shown to contribute to onset, exacerbation and course of several medical disorders, including hypertension, that are worsened by poor emotion regulation, and to prompt maladaptive or unhealthy behaviors (Lumley et al., 2007). Previous studies that have investigated the relationship between alexithymia and hypertension yielded mixed results (Jula et al., 1999; Peters and Lumley, 2007; Consoli et al., 2010; Grabe et al., 2010). In a study by Rafanelli *et al*. (2012), specific psychological profiles emerged using cluster analysis, with patients reporting moderate-to-severe hypertension being more likely to display affective symptomatology and alexithymic features; manifestations of somatization were found to be significantly associated with isolated systolic hypertension.

Interestingly, we found no significant association between allostatic overload and DSM-5 diagnoses. This might be due to the fact that DSM-5 captures only a narrow part of the information needed for the psychological assessment in medical settings, as compared to the DCPR (Guidi et al., 2013; Cosci and Fava, 2016; Piolanti et al., 2019).

Furthermore, we found significantly greater cardiovascular risk among hypertensive patients reporting allostatic overload compared to those who did not, confirming previous findings of increased likelihood of worsened medical outcomes associated with allostatic overload (McEwen and Stellar, 1993; McEwen, 2008; Fava et al., 2019; Gillespie et al., 2019), particularly among hypertensive patients (Mocayar Maròn et al., 2019).

The present study has some limitations, mainly due to its cross-sectional design that does not allow to assess the temporal stability of associations between allostatic overload and both psychological and health variables. The findings should be considered with caution, given the small sample size and variability in disease duration and progression. Nonetheless, it

provides new insights into the clinical relevance of allostatic overload in the development and course of essential hypertension, with important implications for the non-pharmacological management and treatment planning (Rainforth et al., 2007; Solano Lopez, 2018; Williams et al., 2018).

There is a need for a more comprehensive psychological assessment in hypertension, encompassing allostatic overload (Fava et al., 2010, 2017, 2019), psychological well-being (Fava, 2016; Kubzansky et al., 2018), and illness behavior (Sirri et al., 2013). A novel and more advanced assessment method based on clinical grounds, such as the clinimetric approach used in this study, can offer new opportunities for evaluating psychosocial stress in hypertension. Self-rating questionnaires may be particularly useful in a busy medical setting.

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Table 1. Sociodemographic and clinical characteristics of hypertensive patients and normotensive control subjects

Sociodemographic and clinical variables	**Hypertensive patients** (n=80) *Mean (SD)*	**Normotensive controls** (n=80) *Mean (SD)*	t_{158}	*p*
Age (years)	62.18 (8.59)	61.09 (8.33)	.633	.529
	n (%)	*n (%)*	χ^2	*p*
Gender			.000	1.000
Male	43 (53.8)	43 (53.8)		
Female	37 (46.3)	37 (46.3)		
Marital status			4.169	.244
Not married	5 (6.3)	1 (1.3)		
Married	54 (67.5)	63 (78.8)		
Separated/Divorced	5 (6.3)	3 (3.8)		
Widowed	16 (20)	13 (16.3)		
Occupational status			1.345	.334
Employed	14 (17.5)	20 (25)		
Retired/Unemployed	66 (82.5)	60 (75)		
Current use of psychotropic medications	18 (22.5)	13 (16.3)	1.000	.424
Current use of medications	80 (100)	31 (38.8)	70.631	<.001
Smoking	19 (23.8)	18 (22.5)	.035	1.000
Alcohol consumption	19 (23.8)	38 (47.5)	9.838	.003

Substance use	1 (1.3)	1 (1.3)	.000	1.000
Hypertension grading				
High-normal	48 (60)			
Grade 1	10 (12.5)			
Grade 2	10 (12.5)			
Grade 3	4 (5)			
Isolated systolic hypertension	8 (10)			
Absolute cardiovascular risk *				
Low	26 (32.5)			
Moderate	20 (25)			
High	15 (18.8)			
Very high	19 (23.7)			
Weight status				
Normal weight	48 (60)			
Overweight	27 (33.8)			
Obesity	5 (6.2)			
Family history of cardiovascular diseases	32 (40)			
	Mean (SD)	*Range (min-max)*		
Resting heart rate (BPM)	70.28 (11.79)	56-92		
Systolic (mmHg)	126.72 (16.88)	100-170		
Diastolic (mmHg)	74.24 (8.84)	60-90		
Duration of illness (months)	108.20 (101.54)			

1 * *cardiovascular risk estimates were based on the Systematic Coronary Risk Evaluation System (SCORE)*

2

Table 2. Clinimetric criteria for allostatic overload (A through B are required)

Criterion A	The presence of a current identifiable source of distress in the form of recent life events and/or chronic stress; the stressor is judged to tax or exceed the individual coping skills when its full nature and full circumstances are evaluated.
Criterion B	The stressor is associated with one or more of the following features, which have occurred within 6 months after the onset of the stressor: 1. at least two of the following symptoms: difficulty falling asleep, restless sleep, early morning awakening, lack of energy, dizziness, generalized anxiety, irritability, sadness, demoralization; 2. significant impairment in social or occupational functioning; 3. significant impairment in environmental mastery (feeling overwhelmed by the demands of everyday life).

Table 3. Differences between hypertensive patients and normotensive control subjects on dimensional psychological measures

Dimensional psychological measures	Hypertensive patients (n=80) *Mean (SD)*	Normotensive controls (n=80) *Mean (SD)*	$F_{1,155}$	*p*
Clinical Interview for Depression				
Anxiety	6.87 (3.02)	5.01 (1.29)	26.703	<.001
Depression	17.56 (6.09)	12.950 (2.98)	38.640	<.001
Total	65.66 (16.87)	48.74 (8.28)	64.994	<.001
PsychoSocial Index				
Stress	3.79 (2.87)	3.11 (1.93)	2.103	.149
Psychological distress	10.55 (7.29)	6.37 (3.61)	21.500	<.001
Abnormal illness behavior	.975 (1.24)	.538 (.84)	6.615	.011
Well-being	7.09 (1.56)	8.01 (1.22)	17.874	<.001
Symptom Questionnaire				
Anxiety	6.52 (4.78)	3.67 (3.03)	19.588	<.001
Depression	7.21 (4.65)	4.12 (3.67)	20.193	<.001
Somatization	9.42 (5.14)	6.64 (5.01)	11.013	.001
Hostility/Irritability	4.41 (4.72)	2.72 (2.80)	7.050	.009

Table 4. Sociodemographic and clinical characteristics of hypertensive patients with and without allostatic overload

Sociodemographic and clinical variables	Presence of allostatic overload (n=26)	Absence of allostatic overload (n=54)		
	Mean (SD)	*Mean (SD)*	t_{78}	*p*
Age (years)	63.07 (8.35)	61.73 (8.82)	.486	.629
	n (%)	*n (%)*	χ^2	*p*
Gender			.894	.473
Male	12 (46.1)	31 (57.4)		
Female	14 (53.8)	23 (42.6)		
Marital status			.642	.887
Not married	2 (7.7)	3 (5.5)		
Married	16 (61.5)	38 (70.4)		
Separated/Divorced	2 (7.7)	3 (5.5)		
Widowed	6 (23.1)	10 (18.5)		
Occupational status			.080	.763
Employed	5 (19.2)	9 (16.7)		
Retired/Unemployed	21 (80.8)	45 (83.3)		
Current use of psychotropic medications	6 (23.1)	12 (22.2)	.007	1.000

Current use of medications	26 (100)	54 (100)	.000	1.000
Smoking	2 (7.7)	5 (9.2)	.054	1.000
Alcohol consumption	4 (15.4)	15 (27.8)	1.488	.272
Substance use	1 (3.8)	0 (0)	2.103	.147
Hypertension grading			6.068	.194
High-normal	16 (61.5)	31 (57.4)		
Grade 1	1 (3.8)	10 (18.5)		
Grade 2	6 (23.1)	4 (7.4)		
Grade 3	1 (3.8)	3 (5.5)		
Isolated systolic hypertension	2 (7.7)	6 (11.1)		
Absolute cardiovascular risk*			7.695	.007
Low	4 (15.4)	22 (40.7)		
Moderate	5 (19.2)	15 (27.8)		
High	8 (30.8)	7 (13)		
Very high	9 (34.6)	10 (18.5)		
Weight status			4.323	.115
Normal weight	18 (69.2	31 (57.4)		
Overweight	5 (19.2)	21 (38.9)		
Obesity	3 (11.5)	2 (3.7)		
Family history of cardiovascular disease	7 (26.9)	25 (46.3)	3.206	.091

	Mean (SD)	*Mean (SD)*	t_{78}	*p*
Resting heart rate (BPM)	72.48 (13.61)	68.08 (9.40)	1.330	.190
Systolic (mmHg)	121.73 (16.85)	129.17 (16.50)	-1.870	.065
Diastolic (mmHg)	70.15 (7.81)	76.24 (8.68)	-3.026	.003
Duration of illness	77.59 (63.49)	121.11 (111.91)	-1.707	.092

** cardiovascular risk estimates were based on the Systematic Coronary Risk Evaluation System (SCORE)*

Table 5. Differences between hypertensive patients with and without allostatic overload on dimensional psychological measures

Dimensional psychological measures	Presence of allostatic overload (n=26)	Absence of allostatic overload (n=54)			
	Mean (SD)	*Mean (SD)*	$F_{1,66}$	*p*	η^2_p
Clinical Interview for Depression					
Anxiety	8.39 (4.00)	6.15 (2.10)	7.000	.010	.096
Depression	20.77 (5.94)	16.02 (5.59)	13.457	<.001	.169
Total	77.31 (15.44)	60.06 (14.60)	20.379	<.001	.236
PsychoSocial Index					
Stress	4.23 (2.16)	3.57 (3.15)	1.251	.267	.006
Psychological distress	14.15 (8.47)	8.82 (6.00)	14.272	<.001	.178
Abnormal illness behavior	.85 (1.05)	1.04 (1.33)	.414	.522	.019
Well-being	6.15 (1.57)	7.54 (1.36)	16.567	<.001	.201
Symptom Questionnaire					
Anxiety	9.23 (5.01)	5.22 (4.11)	13.590	<.001	.171
Depression	9.80 (4.33)	5.98 (4.32)	12.098	.001	.155
Somatization	11.65 (4.71)	8.35 (5.03)	6.564	.013	.090
Hostility/Irritability	6.00 (5.98)	3.65 (3.81)	3.824	.055	.055