

Estimation of the Risk of Somatization in Hypertensive Patients

Estimación del riesgo de somatización en pacientes hipertensos

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ABSTRACT

Background: Somatization in hypertensive patients affects not only their quality of life but also their adherence to treatment and the physician-patient relationship, constituting an expensive health care issue. The possibility of estimating the risk of somatization in these patients could promote an individualized management of their manifestations.

Objectives: The goal of this study to stratify the risk of somatization in a cohort of patients with essential hypertension and to characterize the hemodynamic variables associated with the risk of somatization in hypertensive patients.

Methods: A total of 120 subjects undergoing cardiovascular risk assessment were prospectively analyzed and classified in: 1) controlled hypertensive group (CHT) (57%, n=68) and 2) normotensive group (NT) (43%, n=52). The risk of somatization was evaluated using the SCL-90-R symptom checklist, and the anxiety and depression scales. The hemodynamic profile was determined using a validated oscillometric method.

Results: The risk of somatization was higher in the CHT group independently of the presence of other emotional disorders. In subjects with higher risk of depression or anxiety, the evidence of somatization was greater ($p < 0.0001$). In the CHT group, those who received treatment (n=38) had greater risk of somatization and of sleep disorders compared to those without treatment in the same group. Body mass index was associated with the risk of somatization ($p = 0.0227$) and female sex was a predictor of somatization, anxiety and depression ($p = 0.001$). A direct relationship was observed between cardiac output and depression and somatization, and between the risk of somatization and the product of heart rate and systolic blood pressure at rest.

Conclusion: The estimation of the risk of somatization is feasible using a validated and reproducible tool. The frequently consulted symptoms in this condition could be associated with a higher risk of somatization, particularly linked with female sex, body mass index, drug therapy, presence of emotional abnormalities as depression and anxiety, and a hyperdynamic pattern.

Key words: Somatoform Disorders - Depression - Anxiety - Hypertension - Vascular Stiffness

RESUMEN

Introducción: La somatización en el paciente hipertenso afecta no solo su calidad de vida, sino también su adherencia al tratamiento y la relación médico-paciente, constituyéndose en un problema sanitario de alto costo, por lo que la posibilidad de determinar el riesgo de somatizar en estos pacientes podría favorecer un manejo individualizado de sus manifestaciones.

Objetivos: Estratificar en una cohorte de hipertensos esenciales el riesgo de somatización y caracterizar las variables hemodinámicas asociadas con el riesgo de somatización en pacientes hipertensos.

Material y métodos: Se analizaron de manera prospectiva 120 individuos que asistieron para la evaluación de su riesgo cardiovascular, que se clasificaron en: 1) grupo de hipertensos controlados (HTC) (57%, n = 68) y 2) grupo control de normotensos (NT) (43%, n = 52). El riesgo de somatización se evaluó con el inventario de síntomas SCL-90-R y las escalas de depresión y ansiedad. El perfil hemodinámico se determinó con un método oscilométrico validado.

Resultados: El riesgo de somatización fue más elevado en el grupo HTC de manera independiente de la presencia de otras alteraciones emocionales. Los individuos con mayor riesgo de depresión y/o ansiedad presentaron mayor evidencia de somatización ($p < 0,0001$). En los HTC tratados (n = 38) se observó mayor riesgo de somatización y de trastornos del sueño respecto de los HTC sin tratamiento. El índice de masa corporal se asoció con el riesgo de somatización ($p = 0,0227$) y el género femenino mostró que es predictivo de somatización, ansiedad y depresión ($p = 0,001$). Se observó una relación directa entre el gasto cardíaco y depresión y somatización y entre el riesgo de somatización y el producto de la frecuencia cardíaca por la presión arterial sistólica en reposo.

Conclusiones: Los resultados muestran la factibilidad de estimar el riesgo de somatización a través de una herramienta validada y reproducible. Los síntomas de consulta frecuente en esta condición podrían estar asociados con un riesgo incrementado de somatización, especialmente vinculado al género femenino, el índice de masa corporal, el tratamiento farmacológico, la presencia de alteraciones emocionales como depresión y ansiedad y el patrón hiperdinámico.

Palabras clave: Trastornos somatoformes- Depresión - Ansiedad - Hipertensión - Rigidez vascular

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Abbreviations

ANX	Anxiety	CHT	Controlled hypertension
DEP	Depression	BMI	Body mass index
DP	Double product	NT	Normotension
HR	Heart rate	BP	Blood pressure
CO	Cardiac output	SOM	Somatization
HTN	Hypertension	PWV	Pulse wave velocity

INTRODUCTION

The impact of emotional factors in the development of diseases in general has been widely studied. Stress, anxiety or depression is associated with proatherogenic phenotypes; on the contrary, positive affections have been linked with lower cardiovascular risk. Tajer (1) describes the main biological aspects especially related with positive affections, beyond the activation of the autonomic nervous system and of catecholamines, and including mechanisms related with the immune system, the HPA axis, lipoprotein metabolism and the renin-angiotensin-aldosterone system, among others. The modulation of these mechanisms would be specific and different according to the individual phenotype, promoting greater or lower levels of cardiovascular vulnerability which could be associated with the psychological concept of resilience or the psychological and cardiovascular ability to adapt to stress. (1-5) In this setting, one could propose that somatization would be related with phenotypes expressing negative affections in a circular process in which disorders of quality of life and of the associated biological mechanisms lead to continuous cardiovascular damage.

In daily clinical or cardiology practice, physicians treating patients with hypertension (HTN) deal with symptoms as headaches, instability, numbness, sleep disorders or general malaise, which, a priori, would not be related with the pathophysiology of high blood pressure (BP) levels. (6-8) In these cases, somatization constitutes an expensive health care issue not only related with resources and complementary tests, but also because it particularly affects the adherence to treatment and the patient's quality of life. (9) The possibility of estimating the risk of somatization in these patients could favor an individualized management of these manifestations, and different validated scales have been evaluated in populations with other conditions. (10) Probably, sympathetic hyperactivity and autonomic system imbalance may be present in these subjects with negative emotions, promoting a hyperdynamic state and, at the same time, modifying the damping mechanisms of the peripheral arteries due to endothelial dysfunction and higher vascular smooth muscle tone, with greater oxidative stress. All these mechanisms contribute to the atherogenic process and, thus, to the risk of developing early cardiovascular disease.

The goal of this study was to stratify the risk of somatization in a cohort of patients with essential HTN, characterize the hemodynamic variables associated with the risk of somatization, and evaluate the corre-

lation between the risk of somatization and emotional abnormalities with the hemodynamic profile in controlled hypertensive patients.

METHODS

The cohort was constituted by 240 consecutive subjects undergoing assessment of their cardiovascular risk in primary prevention at the Centro Médico Santa María de la Salud. Each subject signed an informed consent form and completed the SCL-90-R scale with his/her personal data which were not revealed for data analysis. The properties of arterial wall mechanics were evaluated. Full complete anamnesis and physical examination with baseline and anthropometric data collection were performed. (11)

The following conditions were considered exclusion criteria: uncontrolled HTN, use of antidepressants, previous depression, neoplasms, insufficient answers or technical issues in the evaluation of the instrument, previous diabetes or cardiovascular events detected in the current evaluation.

The SCL-90-R is a self-report data collection instrument developed to assess patterns of symptoms that are present in individual subjects. (11-13) The scale evaluates a person's level of psychological distress over the past week. It can be used in patients undergoing psychological or psychiatric treatments or in the general population without a specific mental disorder.

The instrument consists of 90 items and 9 subscales scored on a five-point scale ranging from 0 to 4. Completion of the questionnaire takes around 15 minutes for a person with primary education level. The scores are calculated by dividing the sum of scores for a dimension by the number of items in the dimension (e.g., somatization subscale). The range of the resultant values is considered and three indexes are determined: global severity index, positive symptom total and positive symptom distress index.

For the purpose of this study, three subscales were selected: somatization (SOM), depression (DEP) and anxiety (ANX).

The SOM subscale reflects distress arising from perceptions of bodily dysfunction (complaints of cardiovascular, gastrointestinal or respiratory system). The DEP dimension reflects a representative range of clinical depression manifestations, as symptoms of dysphoric mood, loss of vital energy, feelings of hopelessness, lack of motivation and possible thoughts of suicide. The ANX subscale evaluates general signs of anxiety as nervousness, tension and dread. If the score obtained in any subscale revealed a high level of symptoms, the patient was interviewed and informed about the results of the questionnaire. During the encounter, the level of awareness of the subject's psychological distress, either anxiety depression or somatization, was firstly evaluated. Then, the presence of stressors experienced by the person lately was explored, as well as the coping strategies and family and social network. Consultation with a psychologist and/or psychiatrist was suggested according to the results of the encounter, depending on the type of case and severity.

The hemodynamic characteristics and the elastic properties of the artery wall were evaluated in a non-invasive fashion. The patients remained in a quiet and comfortable room at 22°C, lying in the supine position for at least 10 minutes. After placing the cuff, a validated oscillometric device was used (Mobil-O-Graph PWA, IEM, Germany), to estimate peripheral and central BP, augmentation index and oscillometric pulse wave velocity (PWV) by means of the ARC Solver method (Austrian Institute of Technology, Vienna, Austria). All the determinations were taken in the non-dominant arm except when contraindicated.

The following determinations were obtained: brachial systolic and diastolic BP, brachial pulse pressure, aortic pressure increase and augmentation index, cardiac output (CO), peripheral vascular resistance index, PWV and heart rate (HR).

Statistical analysis

Continuous variables were expressed as mean (standard deviation) or median (interquartile range) with 95% confidence intervals (for mean or median) as applicable for normal distribution, and percentages for categorical variables. Student's t test was used to compare continuous variables with normal distribution among the subgroups and the Mann-Whitney test for continuous variables with abnormal distribution. Pearson's chi square test was used to evaluate the association between categorical variables (e.g., presence or absence of hypertension).

The Shapiro-Wilk test was applied to test the normality of data. A p value < 0.05 was considered statistically significant. Spearman's correlation coefficient was employed to analyze the association between quantitative variables.

Data processing was performed using R language version 3.2.

Ethical considerations

The study was approved by the institutional Committee of Clinical Studies. All the patients signed an informed consent form to participate, and received information about the characteristics and objectives of the evaluation. The results

were reported individually

RESULTS

After applying exclusion criteria, a total of 120 subjects were included in the study (57±14.8 years, 50% women). The population was divided into two groups: controlled hypertension (CHT) (57%, n=68) and normotension (NT) as control group (43%, n=52) (Table 1).

The mean SCL-90-R score was 113.5±15.9 points; the risk of SOM, DEP and ANX was determined by identifying the scores defined by each subject to the possible answers to each item of the corresponding subscale. The risk of SOM was independently associated with CHT (p<0.0001). DEP was more common in CHT than in NT, independently of SOM (Spearman, p<0.0001) (Figure 1). A relationship between the DEP, ANX and SOM subscales was noted in all the patients. Body mass index (BMI) was associated with the risk of somatization (rho -0.298, p=0.0227) and female sex was a predictor of SOM, ANX and DEP (p=0.001). Age was neither a significant predictor of any of the symptoms analyzed, nor of the prevalence of SOM (rho 0.0072, p=0.938), DEP (rho 0.0268, p=0.669) or ANX (rho -0.039, p=0.775) (see Table 1).

In hypertensive subjects, the incidence of DEP, SOM and sleep disorders was higher in those receiving pharmacological treatment (n=38) compared with those who were not taking antihypertensive drugs and those with NT (Table 1). This association was independent of the type of drug and the number of years since the diagnosis of HTN (without drugs 3.6±1.8 years, with drugs 4.1±1.9 years, p=0.034).

The most prevalent symptoms and manifestations possibly associated with somatization that were interrogated in the SCLR-90 were headache (CHT 55%, NT 54%; p=ns), anhedonia (CHT 68%, NT 21%; p=0.002), feelings of guilt (CHT 32%, NT 9%;

Table 1. Baseline characteristics and distribution of the risk of somatization, depression and anxiety

	Normotension	Hypertensive patients without pharmacological treatment	Hypertensive patients with pharmacological treatment	p
n	52	30	38	
Female, n (%)	28(54)	15(50)	20(53)	0.88
Age, years	55 ±15.1	56 ±12.9	55 ±16.4	0.81
SBP/DBP, mm Hg	115.9 ± 9.325/75.2 ± 6.0	132.1±8.5/82.2 ± 5.9	133.2 ±6.9/84.1 ±5.8	0.01
BMI	24.8	25.2	24.9	0.8
Antihypertensive drugs, number	0	0	2.0 ±1.5	0.67
Somatization	5 ±2.1	7.0±3.2	9.9±4.9	0.01
Depression	10.07 ±5.4	13.1 ± 7.6	16.8 ±5.7	0.01
Anxiety	6.5 ±5.2	7.7 ± 5.6	7.3 ± 5.8	0.07

The study population was classified according to the diagnosis of hypertension in normotension group (NT) and controlled hypertension (CHT), with two subgroups of CHT with or without antihypertensive therapy. The SCL-90-R instrument gives a score to each answer obtained and the final scores identify the risk of the variables analyzed. The table shows the corresponding scores for each variable in the different groups and subgroups of the population. n: Number of patients SBP: Systolic blood pressure. DBP: Diastolic blood pressure. BMI: Body mass index.

$p=0.0001$), dizziness (CHT 71%, NT 15%; $p=0.0001$) and sleep disorders (CHT 42%, NT 27%; $p=0.002$).

A direct relationship was observed between CO and DEP and SOM, ($\rho: 0.3044$, Spearman's correlation coefficient, $p=0.02$), and between peripheral vascular resistance and DEP ($\rho: -0.2812$, $p=0.04$). A positive correlation was observed between the risk of SOM and the rate pressure product at rest ($\rho: 0.38$, $p=0.02$) (Figures 2 and 3).

Central systolic pressure and aortic augmentation index were not associated with any of the psychological variables defined in this study.

DISCUSSION

The present study demonstrates that the risk of SOM in this cohort is related with female gender, HTN under treatment and BMI.

Neuman (14) described HTN as an intrapersonal stressor perceived by the patient as an external influence, and could thus generate a defensive action and maladjustment especially triggered in the face of a lifelong treatment. In most of the studies, the association between negative emotions and psychosocial disorders has been related with the risk of depressive syndrome, as evidenced by its increased incidence after myocardial infarction, and conversely, the risk of cardiovascular disease is higher in subjects with depressive disorder. This bidirectional relationship probably involves the activation of immune-mediated inflammatory mechanisms and autonomic system imbalance which have been described in both entities. The possible secondary effects of the drugs commonly used in cardiology on the risk of depression have been extensively studied. In the same sense, the adverse effects of drugs used in psychiatric disorders on metabolic and cardiovascular balance are also known. The relationship between the risk of somatization and the pharmacological treatment of HTN has not been described in the literature, and it should be clarified whether it could be due to direct effects of the drugs or to the fact that when the subject becomes aware of having a cardiovascular disease, he/she may feel vul-

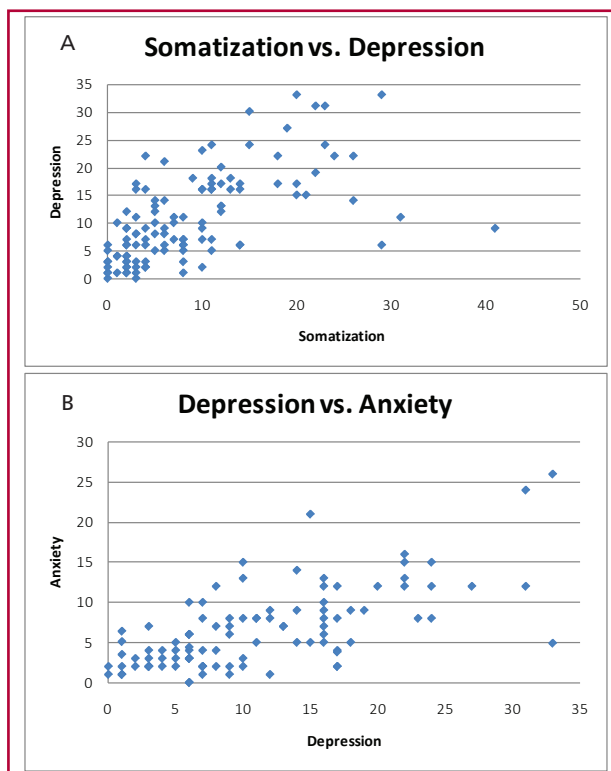


Fig. 1. Distribution of psychological variables. The graphs show the significant relationships between the variables evaluated in all the population: a) somatization and depression (Spearman's correlation coefficient, 0.67, $p<0.0001$); b) depression and anxiety (Spearman's correlation coefficient, 0.71, $p<0.0001$). These relationships would suggest that the risk of somatization could represent the presence of symptoms as a manifestation of an excessive concern towards normal bodily sensations in subjects with higher prevalence of negative emotions detected by this evaluation instrument. The values in the axes represent the scores the SCL-90-R gives to each answer of the items explored.

nerable or experience a traumatic impression.

The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) describes SOM as a chronic pattern of illness behavior with a lifestyle character-

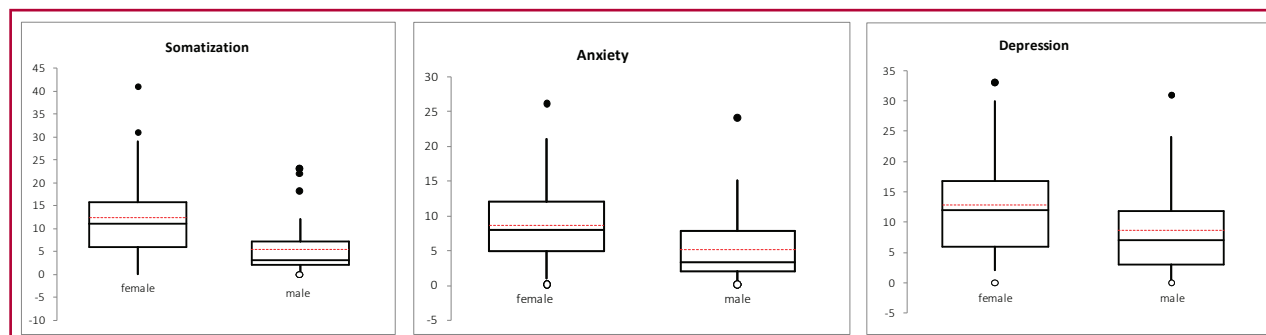


Fig. 2. Distribution of psychological variables by sex and blood pressure levels. Multivariate analysis demonstrated a significant association between female sex and emotional disorders, including the risk of presenting symptoms related with somatization. The negative predictive value of female sex was independent of other population characteristics. The y axis corresponds to the scores of each scale.

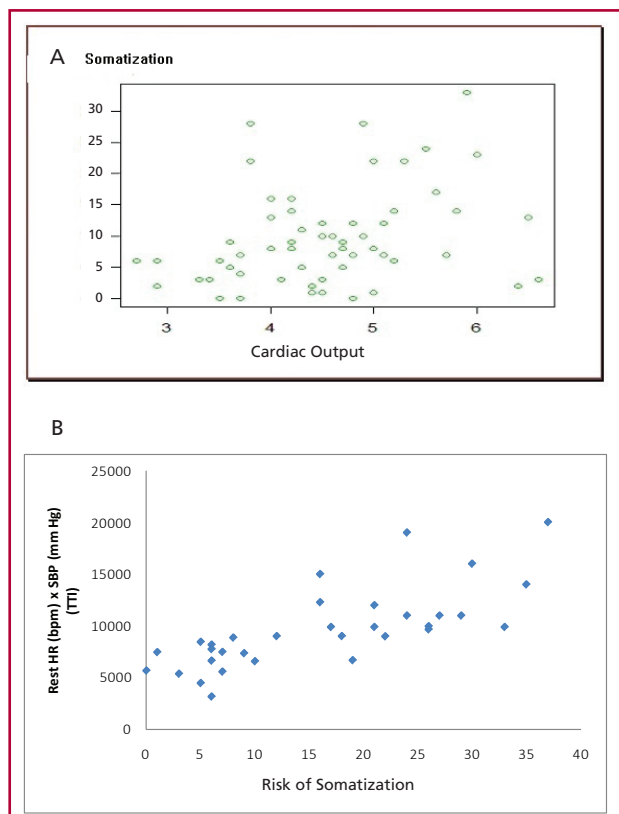


Fig. 3. Hemodynamic characteristics. In the cohort of controlled hypertension, a direct and significant relationship was observed between the estimated cardiac output and the risk of depression ($\rho = 0.3044$, Spearman's correlation coefficient, $p = 0.02$), cardiac output and somatization ($\rho = 0.3201$, $p = 0.02$) (A), and double product (heart rate x systolic blood pressure) at rest and the risk of somatization (B). HR: Heart rate. SBP: Systolic blood pressure. TTI: tension-time index (SBP \times HR).

ized by frequent medical visits and secondary social impairment. (15) Using data from 5 continents, the World Health Organization reported that the prevalence of somatization disorder ranges between 2.7% and 17.7%. (16)

In clinical practice, the diagnosis of the risk of SOM is difficult due to the low availability of diagnostic tools. The results of our study are based on the use of the SCL-90-R SOM, DEP and ANX subscales. There is plenty of evidence about its convergence with other instruments of diagnosis, its concurrent and predictive validity and the reliability of its scales. Even more, there are local scales that validated the scores with those of Argentine populations (Casullo, 2004; Ledesma et al.; 2009). However, and beyond the clinical applicability of the SCL-90-R, this study was not designed to validate the use of the instrument in clinical practice. Our aim was to find strategies to identify the origin of the symptoms commonly related with HTN and the hemodynamic characteristics of the vulnerable subject in an attempt to approach the pathophysiological mechanisms.

SOM may mimic different disorders, as hypochondriasis, in which persons are excessively sensitive to their normal bodily sensations and interpret normal sensations as signs of diseases, seeking unnecessary medical consultations. (17) A person with somatization disorder has few resources for channeling and releasing anxiety. As biopsychosocial human beings, our systems are interrelated, and mutual influence exists between emotions and physical functioning. (8)

The hemodynamic mechanisms detected in this population are consistent with those described as pathophysiological pathways of other emotional disorders in which an imbalance of the autonomic system plays a key role. We could speculate that, in these patients, an autonomic imbalance could be associated with greater cardiovascular risk through immune-mediated inflammatory activation and accelerated atherogenesis. The double product (DP = heart rate \times systolic pressure) is considered an index of cardiac work and has been associated with sympathetic stimulation. In this study, a direct association between DP and the risk of somatization could be suggestive of a hyperdynamic state. However, this hypothesis should be examined in larger studies with more specific evaluations of the autonomous nervous system and the level of sympathetic and parasympathetic stimulation.

CONCLUSIONS

The present study demonstrated that the risk of SOM in a cohort of hypertensive patients was associated with female sex and use of antihypertensive drugs, independently of age and type of drug, and with BMI. The most common hemodynamic pattern showed increased CO and DP at baseline.

Finally, we consider that the main interest of this study could rely on the fact that determining the risk of SOM in hypertensive patients would contribute to the interpretation of symptoms, optimizing the use of diagnostic resources, reducing costs, and improving patient adherence to treatment and quality of life. (18-20).

Conflicts of interest

Kotliar C. has received payment for lectures of the following pharmaceutical laboratories: Astra Zeneca, Ivax, Servier, Baliarda, Novartis, Abbott.

(See author's conflicts of interest forms in the web / Supplementary Material).

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