Hypertension-mediated Cardiac Damage Among Romanian Adult Hypertensive Patients: A Post-hoc Echocardiographic Analysis of the SEPHAR IV Epidemiological Survey

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Abstract

Background: Data regarding cardiac damage in Romanian hypertensive adults are scarce. Our aim was to assess hypertension-mediated subclinical and clinical cardiac damage using a post-hoc echocardiographic analysis of a national epidemiological survey.
Methods: A representative sample of 1477 subjects was included in the SEPHAR IV (Study for the Evaluation of Prevalence of Hypertension and Cardiovascular Risk in an Adult Population in Romania) survey. We retrieved echocardiographic data for 976 subjects, who formed our study group. Cardiac damage included left ventricular (LV) hypertrophy (defined as an LV mass > 95 g/m^2 in females and > 115 g/m^2 in males), coronary artery disease (CAD), and LV diastolic and systolic dysfunction.
Results: Hypertension prevalence was 46.0% in SEPHAR IV and 45.3% in our study subgroup. Hypertensives had a higher prevalence of LV hypertrophy, CAD, diastolic dysfunction (p<0.001 for all) and systolic dysfunction (p=0.03) than normotensives. Age (OR=1.05;95% CI,1.03–1.08;p<0.001), female sex (OR=2.07;95% CI,1.24–3.45;p=0.006), and systolic blood pressure (OR=1.02;95% CI,1.01–1.04;p=0.026) were independent predictors of LVH in hypertensives. Age was a predictor of diastolic dysfunction (OR=1.04;95% CI,1.02–1.06;p<0.001), and female sex was a protective factor against systolic dysfunction (OR=0.26;95% CI,0.10–0.71;p=0.009). Age (OR=1.05;95% CI,1.02–1.07;p<0.001) and dyslipidemia (OR=1.89;95% CI,1.20–3.00;p=0.007) were independent determinants of CAD in hypertensives.
Conclusion: The prevalence of cardiac damage in Romanian hypertensives is high. Both non-modifiable risk factors (such as age and gender) and modifiable (such as dyslipidemia and systolic blood pressure) risk factors are independent predictors of cardiac damage in hypertensives.

Keywords

cardiac damage, hypertension, SEPHAR survey

Rezumat

Context: Există puține date privind afectarea cardiacă în rândul populației hipertensive a României. Scopul studiului a fost evaluarea afectării cardiace clinice și subclinice printr-o analiză ecocardiografică post-hoc a unui studiu epidemiologic național.
Metode: Un eșantion reprezentativ de 1477 subiecți au fost incluși în studiul SEPHAR. Au fost prelucrate date ecocardiografice de la 976 subiecți, care au format lotul de studiu. Afectarea cardiacă a inclus hipertrofia de ventricul stâng (VS) (definită ca un index de masă al VS > 95 g/m^2 la femei și > 115 g/m^2 la bărbați), boala coronariană, disfuncția sistolică și diastolică de VS.
Rezultate: Prevalența hipertensiunii a fost 46.0% în SEPHAR IV și 45.3% în subgrupul de studiu. Hipertensivii au avut o prevalență mai mare a hipertrofiei VS, bolii coronariene, disfuncției diastolice (p<0.001) și disfuncției sistolice (p=0.03). Vârsta (OR=1.05;95% CI,1.03–1.08;p<0.001), sexul feminin (OR=2.07;95% CI,1.24–3.45;p=0.006) și tensiunea arterială sistolică (OR=1.02;95% CI,1.01–1.04;p=0.026) sunt predictori independenți ai hipertrofiei VS la hipertensivi. Vârsta a fost un predictor al disfuncției diastolice (OR=1.04;95% CI,1.02–1.06;p<0.001) iar sexul feminin un factor protector împotriva disfuncției sistolice (OR=0.26;95% CI,0.10–0.71;p=0.009). Vârsta (OR=1.05;95% CI,1.02–1.07;p<0.001) și dislipidemia (OR=1.89;95% CI,1.20–3.00;p=0.007) au fost determinanți independenți ai bolii coronariene la hipertensivi.
Concluzii: Prevalența afectării cardiace la hipertensivii români e ridicată. Atât factori de risc nemodificabili (vârsta și sexul), cât și modificabili (dislipidemia și tensiunea arterială sistolică) sunt predictori independenți ai afectării cardiace la hipertensivi.

Cuvinte cheie

afectare cardiacă, hipertensiune arterială, studiu SEPHAR

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Introduction

Hypertension (HT) remains a major cause of morbidity and mortality worldwide, affecting approximately 1 billion people across the globe and having a higher prevalence in low- and middle-income countries.[1-3] Consequently, lowering blood pressure (BP) is one of the main targets for public health campaigns, since doing so reduces the global vascular risk across all categories of hypertensive patients.[4] HT is a multi-systemic disease, affecting the macro- and microvasculature of every organ – a process referred to as HT-mediated organ damage.[5] The heart is one of the main organs affected by HT: chronic elevation of BP leads to cardiomyocyte hypertrophy and fibrosis, increasing the risk for arrhythmias and atherosclerotic coronary artery disease (CAD), and eventually leading to heart failure (HF).

The SEPHAR (Study for the Evaluation of Prevalence of Hypertension and Cardiovascular Risk in an Adult Population in Romania) project encompassed four cross-sectional national epidemiological studies, held between 2005 and 2021, which shed light upon HT prevalence, treatment, awareness, and control in a country at high cardiovascular risk.[6] However, there are limited data regarding cardiac damage among Romanian hypertensive subjects. We aimed to evaluate the prevalence and determinants of both asymptomatic and clinically overt cardiac damage among the hypertensive population from SEPHAR IV, using a post-hoc echocardiographic analysis.

Methods

1. Study population

Subject selection in SEPHAR IV was completed using a multistratified sampling procedure of Romanian adults aged between 18 and 80 years, who were randomly selected while taking into account the population distribution across territorial regions, rural vs. urban areas, gender, and age groups, according to data from the last national census. The sample selection and methodology have been detailed for the preceding SEPHAR surveys elsewhere.[6,7] In order to ensure a representative population sample, a minimum of 1379 subjects were required. After confirming their participation and providing written informed consent, the subjects were programmed for evaluation in a medically equipped bus, which travelled to each of the study sites, according to the regional schedule of the survey, between May and July 2021.

2. Methodology

Like all the previous SEPHAR editions, SEPHAR IV included two visits that were four days apart, allowing for anthropometric measurements, repeated BP measurements, echocardiographic acquisitions, carotid ultrasound examinations, arterial rigidity evaluation, and the collection of blood and urine samples. This workflow is presented in Figure 1.

For each subject, we recorded the presence of any cardiovascular risk factor and the personal history of myocardial infarction/angina/

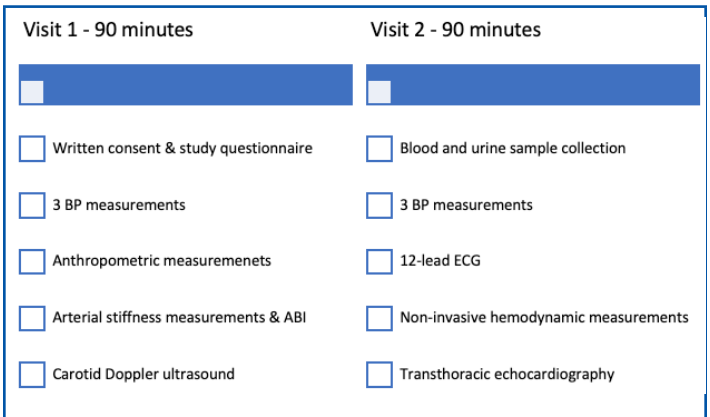


Figure 1 - Study workflow in SEPHAR surveys. ABI – ankle-brachial index; BP – blood pressure; ECG – electrocardiogram

myocardial revascularization. Atrial fibrillation was diagnosed either based on ECG documentation at the time of the study visit or on previous history of atrial fibrillation. BP measurements were performed using an automatic device certified by the Association for the Advancement of Medical Instrumentation, with an adjustable cuff for arm circumferences from 24 to 42 cm, according to the current European Society of Hypertension (ESH) guidelines for BP measurement.[8] At each study visit, three BP measurements were performed one minute apart from one another, and the average BP for each visit was defined as the mean of the second and third BP measurement, without taking into consideration the first one. A subject was considered hypertensive if he had a systolic BP ≥ 140 mm Hg and/or a diastolic BP ≥ 90 mm Hg at both visits, or if he had been previously diagnosed with HT and received medication during the last 2 weeks prior to enrolment, irrespective of the BP values found at the study visits.

3. Echocardiography

Standard transthoracic acquisitions, ECG-gated, were performed over three cardiac cycles for patients in sinus rhythm, and over five cycles for patients in atrial fibrillation. Two-dimensional, color Doppler, and spectral Doppler techniques were used to assess the morphology and function of the left ventricle (LV) and the left atrium (LA). The thickness of the interventricular septum (IVS), the LV posterior wall, and the LV diameter were measured at end-diastole from the parasternal long-axis window. LV mass was calculated using 2D mode and the Devereux formula from the parasternal short-axis window, according to current recommendations, and it was subsequently indexed to body surface area.[9] LV hypertrophy (LVH) was defined as an indexed LV mass > 95 g/m^2 in females and > 115 g/m^2 in males.[9] Based on the LV mass index and LV relative wall thickness (RWT), we further divided the type of LV remodelling into four patterns: normal geometry (RWT≤ 0.42 and normal LV mass), concentric remodelling (RWT>0.42 and normal LV mass), eccentric hypertrophy (RWT≤ 0.42 and increased LV mass) and concentric hypertrophy (RWT>0.42 and increased LV mass).[9]

LV diastolic function was evaluated using the transmitral diastolic flow assessed with pulsed wave Doppler, the dimensions of the LA,

and the maximal velocity of the tricuspid regurgitation jet, according to current guidelines.[10] Based on the proposed algorithms,[10] the subjects were categorized as having normal diastolic function; indeterminate diastolic function; or first-degree, second-degree, or third-degree diastolic dysfunction. Left ventricular ejection fraction (LVEF) was measured using the Simpson biplane method in the apical four- and two-chamber views. Systolic dysfunction was defined as a LVEF < 54% in females and <52% in males.[9] A subject was considered to have HF if he had either diastolic dysfunction with clinical signs and/or symptoms of HF, or LV systolic dysfunction.

LV wall motion abnormalities were assessed in the apical four, two-, and three- chamber views. The presence of CAD was defined by either one of the following criteria:

- Clinical: history of myocardial infarction/angina pectoris/ myocardial revascularization (by percutaneous coronary intervention or coronary artery bypass graft)
- 12-lead ECG: pathological Q waves or ischemic ST segment – T wave changes
- Echocardiography: presence of segmental wall motion abnormalities

Cardiac damage in our study cohort was defined by the presence of LVH, HF (with either reduced or preserved LVEF) or CAD. LVH was considered a subclinical form of HT-mediated organ damage, while CAD and HF were considered clinically overt forms of target organ damage.

4. Missing value imputation

Due to various reasons, the echocardiographic data collected during SEPHAR IV were incomplete for approximately 27% of the subjects. In order to fill in the missing information, we used an ensemble missing value imputation (MVI) method. This technique involves analysing the performance of the most common MVI algorithms and selecting the best three, their outcomes being afterwards combined to obtain the final imputing values. For this study, we have taken into consideration the following methods: Mean Imputation, k-Nearest Neighbours,[11] Multiple Imputation by Chained Equations,[12] Expectation Maximization,[13] Iterative Imputer,[14] and DataWig.[15] The experiments have been conducted on a dataset created by combining echocardiographic data from SEPHAR III and SEPHAR IV, with values eliminated at random to match the 27% missing value rate. From the experiments, the best three MVI algorithms were k-Nearest Neighbours, Iterative Imputer and DataWig. The final imputed values have been determined as the average outcomes for continuous variables, and as the most predicted class for categorical variables.

5. Statistical analysis

Analysis was performed using the SPSS 20.0 statistical software package. Data normality was assessed using the Kolmogorov-Smirnov test. Continuous data were displayed as mean ± standard deviation if normally distributed, and as median (interquartile range) otherwise, and they were compared with Student's t test or Mann-Whitney U test, as dictated by distribution. Categorical data were displayed as number (percentages) and they were compared using a chi-square test or Fisher exact test, depending on normality. Multivariable logistic regression was performed to assess the ability of different parameters to predict HT-mediated cardiac damage. A two-tailed p-value < 0.05 was considered statistically significant.

3. Results

Out of the 1477 subjects enrolled in SEPHAR IV, echocardiographic data were retrieved for 976 subjects, of whom 263 had incomplete data and were submitted to missing value imputation. All the 976 subjects were then included in our analysis. There were 396 (40.6%) males and 580 (59.4%) females in our study population and the mean age was 50.8 (16.6) years. There were 442 (45.3%) hypertensive subjects in our study group, 356 (80.5%) of whom were known hypertensives, and 86 (19.5%) of whom were newly diagnosed at the time of the survey. These numbers are similar to those obtained when analysing the whole SEPHAR IV population, who had a hypertension prevalence of 46.0% (n=680), with 81.0% known hypertensives (n=551) and 19.0% (n=129) newly diagnosed – results which are to be published elsewhere.

The main clinical and echocardiographic characteristics of our selected population are displayed in Table 1. Of all the hypertensive subjects with diabetes, 61 (83.6%) were receiving antidiabetic treatment. On the other hand, of all the hypertensive subjects with dyslipidaemia, only 79 (37.3%) were taking some type of hypolipemiant medication.

The prevalence of LVH among hypertensives was 30.8%. Regarding the LV remodelling pattern, 202 (45.7%) of the hypertensive subjects had normal LV geometry, 104 (23.5%) had concentric remodelling, 73 (16.5%) had eccentric LVH, and 63 (14.3%) had concentric LVH. Among normotensive subjects, 368 (68.9%) had normal LV geometry, 115 (21.6%) had concentric remodelling, 30 (5.6%) had eccentric LVH, and 21 (3.9%) had concentric LVH ($p<0.001$).

While the mean LVEF in the study group was preserved, it did show significantly lower values in the hypertensive population when compared to normotensive subjects ($p<0.001$). The prevalence of HF, with either preserved or reduced LVEF, among hypertensives was 13.3%. Systolic dysfunction was present in 27 (6.1%) hypertensives. Diastolic dysfunction was observed in 218 (49.3%) of the hypertensive subjects, but only 32 (14.7%) of those also had signs and/or symptoms of HF. CAD was present in 148 (33.5%) hypertensive subjects and 55 (10.3%) normotensive subjects ($p<0.001$), and it was mostly diagnosed based on medical history and ECG changes. Atrial fibrillation was significantly more prevalent among hypertensives (12.4% versus 4.7%, $p<0.001$).

The comparison between hypertensives with and without cardiac damage is displayed in Tables 2-4.

We performed binary logistic regression in order to establish the ability of different risk factors to predict cardiac damage in hypertensive subjects. The multivariable model was constructed using risk factors that showed significant differences between

Table 1 - Clinical and echocardiographic characteristics of the study population.

	All subjects (n=976)	Hypertensive subjects (n=442)	Normotensive subjects (n=534)	p-value
Female, n (%)	580 (59.4%)	248 (56.1%)	332 (62.2%)	0.055
Age (years)	50.8 (16.6)	60.2 (13.0)	43.0 (15.1)	<0.001
Rural residence, n (%)	456 (46.7%)	230 (52.1%)	226 (42.3%)	0.002
Active smoking, n (%)	276 (28.3%)	93 (21.0%)	183 (34.3%)	<0.001
Dyslipidemia, n (%)	341 (34.9%)	212 (48.0%)	129 (24.2%)	<0.001
Diabetes, n (%)	91 (9.3%)	73 (16.5%)	18 (3.4%)	<0.001
Obesity, n (%)	391 (40.1%)	236 (53.4%)	155 (29.0%)	<0.001
Obstructive sleep apnea, n (%)	28 (2.9%)	17 (3.8%)	11(2.1%)	0.10
Systolic BP (mm Hg)	129 (19)	141 (17)	119 (12)	<0.001
Diastolic BP (mm Hg)	83 (10)	88 (11)	78 (8)	<0.001
IVS (mm)	9 (1)	10 (1)	9 (1)	<0.001
LVPW (mm)	9 (1)	10 (1)	9 (1)	<0.001
LVEDD (mm)	45 (5)	46 (5)	44 (5)	<0.001
LVESD (mm)	34 (6)	35 (6)	33 (5)	<0.001
LA diameter (mm)	34 (5)	36 (5)	32 (5)	<0.001
Indexed LV mass (g/m^2)	84 (24)	94 (25)	76 (20)	<0.001
LVH, n (%)	187 (19.2%)	136 (30.8%)	51 (9.6%)	<0.001
Mitral E/A wave ratio	1.23 (0.40)	1.08 (0.37)	1.35 (0.37)	<0.001
Diastolic dysfunction		<0.001		
First degree, n (%)	268 (27.5%)	174 (39.4%)	94 (17.6%)	
Second degree, n (%)	87 (8.9%)	40 (9.0%)	47 (8.8%)	
Third degree, n (%)	6 (0.6%)	4 (0.9%)	2 (0.4%)	
Systolic dysfunction, n (%)	44 (4.5%)	27 (6.1%)	17 (3.2%)	0.03
LVEF (%)	58 (4)	57 (4)	59 (4)	<0.001
Atrial fibrillation, n (%)	80 (8.2%)	55 (12.4%)	25 (4.7%)	<0.001

Continuous data are displayed as mean ± standard deviation. Categorical data are displayed as number (percentages). Units of measurement are given in parentheses. BP – blood pressure; IVS – interventricular septum; LA – left atrium; LV – left ventricle; LVEF – left ventricular ejection fraction; LVEDD – left ventricular end-diastolic diameter; LVESD – left ventricular end-systolic diameter; LVH – left ventricular hypertrophy; LVPW – left ventricular posterior wall; N – number.

Table 2 - Characteristics of hypertensive subjects with and without LVH

	Hypertensives with LVH (n=136)	Hypertensives without LVH (n=306)	p-value
Female, n (%)	93 (68.4%)	155 (50.7%)	<0.001
Age (years)	66.1 (10.3)	57.6 (13.2)	<0.001
Rural residence, n (%)	66 (48.5%)	164 (53.6%)	0.33
Active smoking, n (%)	20 (14.7%)	73 (23.9%)	0.03
Dyslipidemia, n (%)	68 (50.0%)	144 (47.1%)	0.57
Diabetes, n (%)	33 (24.3%)	40 (13.1%)	0.003
Obesity, n (%)	71 (55.9%)	165 (53.9%)	0.70
Obstructive sleep apnea, n (%)	6 (4.4%)	11 (3.6%)	0.68
Systolic BP (mm Hg)	145 (18)	138 (17)	<0.001
Diastolic BP (mm Hg)	88 (11)	88 (10)	0.99

Continuous data are displayed as mean ± standard deviation. Categorical data are displayed as number (percentages). Units of measurement are given in parentheses. For abbreviations see Table 1.

hypertensives with and without cardiac damage: age, sex, smoking, history of diabetes, history of dyslipidemia, history of obstructive sleep apnea, systolic BP, and diastolic BP. The results are shown in Table 5. Age was an independent predictor of LVH, diastolic dysfunction, and CAD in our hypertensive population (p<0.001 for all). Hypertensive females were twice more likely to have LVH and four times less likely to have systolic LV dysfunction. Dyslipidaemia and obstructive sleep apnoea proved to be independent predictors for CAD, while systolic BP was an independent predictor of LVH.

We performed multinomial logistic regression using the same covariates as in the multivariable binary logistic model to identify predictors for a certain pattern of LV remodelling. We found that age was an independent predictor and male sex was a protective factor for either type of geometric remodelling (Table 6).

Table 3 - Characteristics of hypertensive subjects with and without LV dysfunction

	Hypertensives with DD (n=218)	Hypertensives without DD (n=224)	p-value	Hypertensives with SD (n=27)	Hypertensives without SD (n=415)	p-value
Female, n (%)	122 (56.0%)	126 (56.3%)	0.95	7 (25.9%)	241 (58.1%)	0.001
Age (years)	63.3 (10.6)	57.2 (14.3)	<0.001	64.2 (14.1)	59.9 (12.9)	0.13
Rural residence, n (%)	103 (47.2%)	127 (56.7%)	0.047	8 (29.6%)	222 (53.5%)	0.02
Active smoking, n (%)	45 (20.6%)	48 (21.4%)	0.84	8 (29.6%)	85 (20.5%)	0.26
Dyslipidemia, n (%)	107 (49.1%)	105 (46.9%)	0.64	14 (51.9%)	198 (47.7%)	0.68
Diabetes, n (%)	45 (20.6%)	28 (12.5%)	0.02	9 (33.3%)	64 (15.4%)	0.02
Obesity, n (%)	123 (56.4%)	113 (50.4%)	0.21	11 (40.7%)	225 (54.2%)	0.17
OSA, n (%)	9 (4.3%)	8 (3.6%)	0.76	0 (0%)	17 (4.1%)	0.61
Systolic BP (mm Hg)	142 (18)	139 (16)	0.056	142 (22)	140 (17)	0.64
Diastolic BP (mm Hg)	88 (11)	88 (10)	0.47	88 (14)	88 (10)	0.96

Continuous data are displayed as mean ± standard deviation. Categorical data are displayed as number (percentages). Units of measurement are given in parentheses. DD – diastolic dysfunction; OSA – obstructive sleep apnea; SD – systolic dysfunction. For other abbreviations see Table 1.

Table 4 - Characteristics of hypertensive subjects with and without CAD

	Hypertensives with CAD (n=148)	Hypertensives without CAD (n=294)	p-value
Female, n (%)	78 (52.7%)	170 (57.8%)	0.31
Age (years)	64.9 (12.2)	57.8 (12.7)	<0.001
Rural residence, n (%)	84 (56.8%)	146 (49.7%)	0.16
Active smoking, n (%)	30 (20.3%)	63 (21.4%)	0.78
Dyslipidaemia, n (%)	88 (59.5%)	124 (42.2%)	<0.001
Diabetes, n (%)	37 (25.0%)	36 (12.2%)	<0.001
Obesity, n (%)	76 (51.4%)	160 (54.4%)	0.54
Obstructive sleep apnoea, n (%)	10 (6.8%)	7 (2.4%)	0.02
Systolic BP (mm Hg)	142 (19)	139 (17)	0.19
Diastolic BP (mm Hg)	87 (11)	89 (11)	0.14

Continuous data are displayed as mean ± standard deviation. Categorical data are displayed as number (percentages). Units of measurement are given in parentheses. CAD – coronary artery disease.

Table 5 - Multivariable logistic regression analysis for predictors of various forms of cardiac damage

	LVH		Diastolic dysfunction		Systolic dysfunction		CAD	
Variable	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	1.05 (1.03-1.08)	**<0.001**	1.04 (1.02-1.06)	**<0.001**	1.04 (0.99-1.08)	0.115	1.05 (1.02-1.07)	**<0.001**
Female sex	2.07 (1.24-3.45)	**0.006**	1.10 (0.71-1.69)	0.681	0.26 (0.10-0.71)	**0.009**	0.72 (0.45-1.14)	0.161
Dyslipidemia	1.20 (0.74-1.96)	0.465	0.98 (0.65-1.50)	0.941	1.31 (0.52-3.31)	0.564	1.89 (1.20-3.00)	**0.007**
Diabetes	1.63 (0.87-3.04)	0.127	1.31 (0.74-2.33)	0.361	2.20 (0.82-5.88)	0.117	1.52 (0.85-2.71)	0.161
Smoking	0.90 (0.64-1.25)	0.514	1.27 (0.97-1.67)	0.082	1.30 (0.72-2.35)	0.393	1.04 (0.77-1.40)	0.804
OSA	1.25 (0.41-3.86)	0.697	0.96 (0.33-2.76)	0.935	1.00 (0.99 -1.01)	0.998	0.30 (0.10-0.94)	**0.039**
Systolic BP	1.02 (1.01-1.04)	**0.026**	1.01 (0.99-1.02)	0.433	1.00 (0.97-1.03)	0.957	1.00 (0.99-1.02)	0.621
Diastolic BP	1.00 (0.97-1.03)	0.886	1.00 (0.98-1.03)	0.985	1.00 (0.94-1.06)	0.905	1.00 (0.97-1.03)	0.730

BP – blood pressure; CAD – coronary artery disease; CI – confidence interval; LVH – left ventricular hypertrophy; OR – odds ratio; OSA – obstructive sleep apnea. Bolded p-values are statistically significant.

4. Discussion

The results of our study can be summarized as follows: (1) cardiac damage, both subclinical (LVH) and clinical (CAD, HF with reduced or preserved LVEF) is significantly more prevalent among hypertensive than among normotensive subjects in the Romanian adult population; (2) age, female sex and systolic BP are independent predictors of LVH in hypertensives, with age and sex being predisposing factors for either type of LV geometric remodelling; (3) age is a predictor of diastolic dysfunction and male sex a predictor of systolic dysfunction among hypertensives; (4) age, dyslipidaemia and obstructive sleep apnoea are independent determinants of CAD in hypertensives.

The chronic elevation of BP in hypertensives determines adaptive myocardial structural and functional changes, such as cardiomyocyte hypertrophy, fibrosis, and stiffening – a process which is mediated by genetic and neuro-humoral factors.[16-18] These

Table 6 - Multinomial logistic regression for predicting various patterns of LV remodelling

Pattern of LV remodelling	Risk factor	B	SE	p	OR (95% CI)
Concentric remodelling	Age	0.027	0.012	0.026	1.028 (1.003 – 1.052)
	Male sex	-0.731	0.281	0.009	0.481 (0.278 – 0.834)
Eccentric hypertrophy	Age	0.064	0.017	<0.001	1.066 (1.030 – 1.103)
	Male sex	-0.976	0.355	0.006	0.377 (0.188 – 0.755)
Concentric hypertrophy	Age	0.056	0.018	0.002	1.058 (1.021 – 1.096)
	Male sex	-1.131	0.376	0.003	0.323 (0.154 – 0.675)

The reference category is normal LV geometry. Model fitting information: Chi-square=90.23; p<0.001; Cox & Snell=0.201; Nagelkerke=0.218; McFadden=0.089; B – regression coefficient; SE – standard error; OR – odds ratio; CI – confidence interval.

subclinical changes can progress to clinically overt cardiac disease, such as HF, arrhythmias, and CAD. All of these forms of cardiac damage carry prognostic implications, since it is well established that hypertensives with cardiac damage have an increased risk of all-cause death.[19]

We assessed the presence of LV remodelling by 2D echocardiography in our study in line with current recommendations, since cardiac imaging has higher sensitivity and specificity than an electrocardiogram for the detection of LVH.[20] 54.3% of the hypertensive subjects from our cohort had abnormal LV geometry; this prevalence is higher than that reported by Milani et al. in Caucasian hypertensives, which was only 46%.[21] Acknowledging this high prevalence of LV remodelling in Romanian hypertensives is important since all forms of altered geometry (including concentric remodelling) carry a high risk of adverse events.[22]

Cuspidi et al. showed in a systematic review that the prevalence of LVH among hypertensives is between 36% and 41%, depending on the criteria used for defining LVH.[23] In fact, the actual prevalence of LVH varies widely with the clinical characteristics of the studied population.[24] It is well known from the Framingham Heart Study that LVH is more prevalent in women,[25] an observation that has been confirmed by recent studies as well,[26] and which is in line with our findings. Ethnicity also plays an important role in the development of LVH; for example, Black people have a much higher incidence of LVH than white people,[27] while a study from China reported a 20.2% prevalence of LVH in untreated Chinese hypertensives.[28] In our study, the prevalence of LVH among Romanian adult hypertensives was 30.8%; these results are similar with a recent study from Nigeria, which found a 32.4% prevalence of LVH in a cohort of African hypertensives.[29] Interestingly enough, in the previous SEPHAR survey from 2016, the prevalence of echo-derived LVH in the Romanian hypertensive population was much lower at 22.9%,[30] despite similar rates of BP control in the two survey editions (30.8% in SEPHAR III,[6] 30.9% in the current study). This highlights the importance of identifying predictors for the development of subclinical cardiac damage. In our study, age, female sex, and systolic BP were independent determinants of LV hypertrophy; similar findings were reported by Li et al., who also found that body mass index, together with age, female sex, and systolic BP, independently predicted LVH.[28]

The prevalence of diastolic dysfunction in European general populations ranges from 20.2% to 27.3%, according to published data,[31,32] while the prevalence of diastolic dysfunction was 37% in our study sample. Among hypertensives, diastolic dysfunction appears early, even before the onset of abnormal LV remodelling,[33] and it is a strong independent predictor of major adverse events.[34] In our cohort of 442 hypertensives, the prevalence of diastolic dysfunction was 49.3%. Published studies regarding diastolic dysfunction among hypertensives usually enrolled small numbers of patients, between 90 and 157,[33,35,36] and found a prevalence between 35.6% among Saudi Arabian hypertensives[35] and 65% among hypertensives from Portugal.[36] One probable explanation for such discrepancies is the use of different definition criteria for diastolic dysfunction. A larger study from Poland enrolled 610 hypertensives and found a prevalence of diastolic dysfunction of 50.3%,[37] which is similar to our findings. Cardiac damage appears to vary widely according to the studied population, which highlights the need for epidemiological research enrolling specific population samples.

The prevalence of systolic dysfunction in the general population has decreased in the last 3 decades, while the prevalence of diastolic dysfunction and HF with preserved EF has increased.[38-39] Among hypertensives, studies investigating the prevalence of systolic dysfunction are scarce, since HT usually leads to diastolic dysfunction, and to a lesser extent to systolic LV dysfunction, with the latter particularly seen in patients who also have a history of myocardial ischemia/infarction.[40] Published data found that systolic dysfunction had a prevalence between 3.6%[41] and 6.7%[42]. Independent predictors of systolic dysfunction were male sex, diabetes and larger LV mass.[42] In our study, the prevalence of systolic dysfunction among hypertensives was 6.1%, higher than the prevalence reported in SEPHAR III< of 4.4%[30]; however, the cut-off for defining systolic dysfunction in the previous SEPHAR survey was a LVEF<50% in both males and females, which is slightly different from the latest recommendations of chamber quantification that have been used in the current study[9].

HT is a well-established modifiable risk factor for myocardial ischemia, and the prevalence of atherosclerotic lesions of the major coronary arteries among hypertensives is up to 34%[43]. It's not entirely clear why some hypertensive patients develop atherosclerotic lesions of the coronary bed, while others do not, but it is most probably related to the interaction between HT and other modifiable risk factors for CAD, such as smoking, diabetes, or dyslipidemia. In our study, the prevalence of CAD in hypertensives was 33.5%, slightly higher than in SEPHAR III, where the reported

prevalence of CAD was 32.1%[30]. Age and dyslipidemia were independent predictors of CAD in our study cohort, while other major cardiovascular risk factors (such as smoking and diabetes) were not. A possible explanation for this is that we did not include in our analysis the "former smoker" status, but only the "active smoker" one. 83.6% of the diabetic patients were receiving antidiabetic treatment at the time of the survey, which might have attenuated the predictive power of diabetes as a risk factor for CAD in our analysis. By comparison, only 37.3% of all dyslipidemic patients were on hypolipemiant drugs, and hypertensives with dyslipidemia had almost a two-fold higher risk of CAD when compared to hypertensives without dyslipidemia.

Study limitations

As we previously stated, this study is a post-hoc analysis of a cross-sectional national epidemiological survey designed to assess the prevalence of HT and major cardiovascular risk factors in the adult population of Romania, and not the prevalence of HT-mediated cardiac damage. Another major limitation is the fact that only standard echocardiographic techniques were used in the acquisitions; the use of Tissue Doppler imaging or speckle-tracking analysis would have probably reclassified some patients from normal LV function to systolic and/or diastolic dysfunction. Finally, some of the echocardiographic data were incomplete, a limitation which was overcome using MVI algorithms.

Conclusion

The prevalence of HT-mediated cardiac damage, both subclinical and clinical, among the hypertensive adult population of Romania is high; moreover, it appears to be rising when compared with the previous national epidemiologic survey. Both non-modifiable risk factors (such as age and gender) and modifiable (such as dyslipidemia and systolic blood pressure) risk factors were independent predictors of cardiac damage among hypertensives. These results highlight the importance of therapeutic strategies aimed not only to adequately control BP, but also to diminish HT-mediated organ damage.

Conflict of interest

none declared.

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