Επίκαιρο Άρθρο

Cardiac damage in hypertensive patients. The Romanian experience

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ABSTRACT

Hypertension is a major cause of morbidity and mortality worldwide. The progression of hypertension leads to target organ damage, mainly in the heart, kidney and brain. The aim of this paper is to discuss the cardiac damage among hypertensive population, while putting into context the results of a Romanian epidemiological survey (SEPHAR III), which assessed the HT-induced target organ damage in the adult population of a country at high cardiovascular risk.

Key-words: hypertension, target organ damage cardiac damage, cardiovascular risk

INTRODUCTION

Hypertension (HT) remains the leading cause of morbidity and mortality in the western world, affecting approximately 1 billion people worldwide[1]. It is considered the most common modifiable risk factor for atherosclerotic cardiovascular (CV) disease and it frequently coexists with other CV risk factors such as smoking, diabetes and dyslipidaemia[2]. Consequently, HT is one of the main targets for public health campaigns of CV prevention[3]. One of the explanations for the significant morbi-mortality of HT is the fact that it is a multi-systemic disease, potentially affecting the macro- and microvasculature of every organ – a process usually referred to as HT-induced target organ damage[4].

Cardiac damage in hypertension

The heart is one of the main organs affected by HT. The chronic elevation of blood pressure (BP) initially leads to asymptomatic structural and functional myocardial changes such as cardiomyocyte hypertrophy and fibrosis, which subsequently will progress to clinically overt cardiac disease – left ventricular (LV) systolic and diastolic dysfunction, cardiac arrhythmias, coronary artery disease (CAD) and heart failure (HF). LV hypertrophy (LVH) develops as an adaptative process to increased afterload, which is mediated by sympathetic activation[5], endothelin[6], angiotensin II[7] and genetic predisposition[8]. The prevalence of LVH among hypertensive patients is reported to be up to 40%[9] and LVH has been shown to be associated with higher risk of cardiovascular events and death[10].

Increased pressure overload leading to a stiffened hypertrophied LV will progress to LV diastolic dysfunction, increased LV filling pressures, dilatation and fibrosis of the left atrium (LA) and pulmonary congestion, which will determine clinically overt cardiac disease, mainly CAD, atrial fibrillation and HF with either preserved (HFpEF) or reduced ejection fraction (HFrEF)[11]. HT is a well-known independent risk factor for CAD, while almost 50% of the patients with CAD are hypertensive[12]. This is explained by the fact that chronically elevated BP increases endothelial stress, leads to microvascular dysfunction and promotes atherogenesis[13]. The coexistence of HT and CAD increase the risk for the development of HF, through neurohormonal activation[11,14]. Concentric LVH usually leads to HFpEF, while eccentric LVH usually leads

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to HFrEF[4]. HT is also an established risk factor for cardiac arrhythmias, the most common being atrial fibrillation[15]. The increased LA pressure secondary to impaired filling of the hypertrophied LV will lead to LA remodelling and fibrosis, with further development of multiple micro- re-entrant circuits, which will lead to atrial fibrillation[16].

The Romanian experience – the SEPHAR project

In Romania, HT and its complications determine more than 60% of total deaths[17]. Therefore, early diagnosis, HT awareness and optimal BP control, as well as primary prevention strategies are mandatory. The lack of representative epidemiological data regarding the prevalence of the main CV risk factors in the adult Romanian population led to the "Study for the Evaluation of Prevalence of Hypertension and cArdiovascular risk in Romania" (SEPHAR).

The SEPHAR project, which started in 2005, encompassed three epidemiological surveys (with a fourth one currently ongoing), which aimed to assess the prevalence of HT and other cardiovascular (CV) risk factors in Romania, as well as the trend in HT prevalence, treatment and optimal control. SEPHAR III, which was held in 2016, was particularly focused on assessing the prevalence of HT-induced target organ damage. The methodology of the study encompassed two medical visits, four-days apart, which allowed repeated BP measurements according to current guidelines[18], anthropometric measurements, laboratory workup, measurements of arterial stiffness, 12-lead electrocardio-graphic (ECG) tracings, as well as transthoracic echocardiography (TTE) and carotid doppler ultrasound.

The cardiac organ damage was assessed by means of 12-lead ECG and TTE. The vascular damage was evaluated by measuring arterial stiffness parameters, the ankle-brachial index and by performing carotid ultrasound examinations. The renal damage was assessed by measuring the urinary albumin-to-creatinine ratio and by estimating the glomerular filtration rate. On 12-lead ECG tracings we assessed the rhythm and the heart rate, we measured the duration of the PR interval and the QRS complex, we evaluated the presence of conduction disturbances, ST segment-T wave changes, pathological Q waves or LVH criteria such as the Cornell product or the Romhilt Estes score. On TTE we calculated the LV mass, the LV diameters

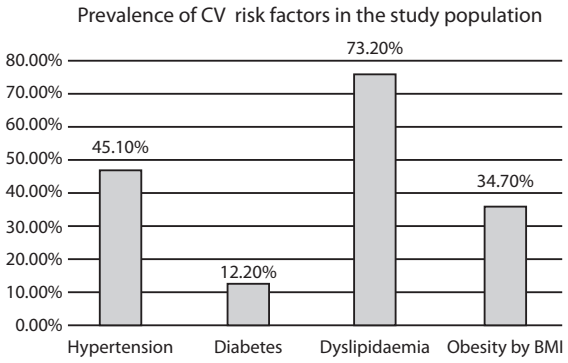

Figure 1. *Prevalence of CV risk factors in the SEPHAR III population.*

and wall thickness, the LV ejection fraction (LVEF) by Simpson biplane method and the LA volume. The study was undergone using a medically equipped bus, which traveled throughout the country, allowing the enrollment of a representative population sample of 2124 subjects, aged between 18 and 80, of which 1970 subjects represented the final study population. The survey confirmed that Romania is indeed a country at high CV risk, with a high prevalence of all the main CV risk factors among the adult population (Figure 1).

Cardiac damage in our study population was defined as the presence of either LVH, CAD, atrial fibrillation or HF. LVH was diagnosed using either ECG criteria (such as the Cornell product>2.440 mm x ms or the Romhilt Estes score>5 points) or echocardiographic criteria, such as LV mass >105 g/m^2 in males (>95 g/m^2 in females)[19]. Both the Cornell product and Romhilt Estes score, as well as echocardiographic LV mass were significantly higher among the hypertensive population from the study group when compared to normotensive sub-

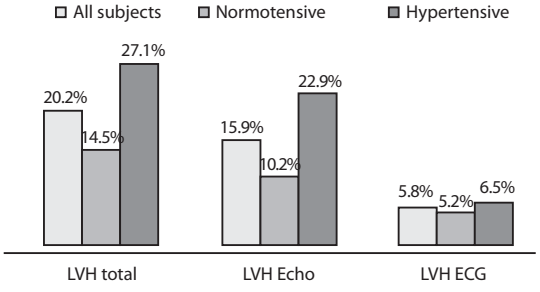

Figure 2. *Prevalence of LVH in the SEPHAR III population. LVH Echo – LVH diagnosed with echocardiographic criteria; LVH ECG – LVH diagnosed with ECG criteria; LVH total – LVH diagnosed by either ECG or echocardiographic criteria.*

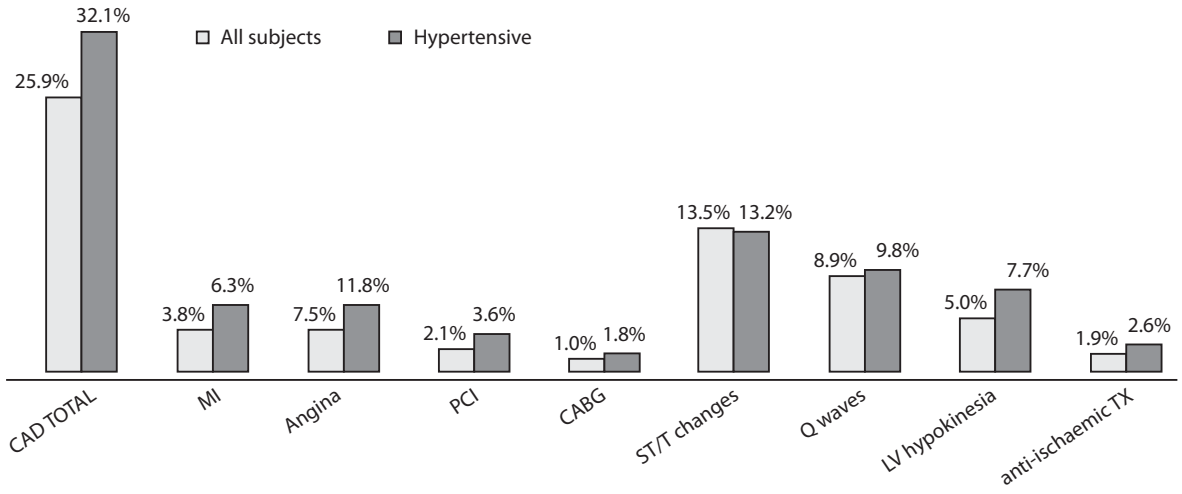

Figure 3. *Prevalence of coronary artery disease in the SEPHAR III population.*

jects ($p<0.0001$, $p=0.006$ and $p<0.0001$, respectively). LVH, defined by either of the ECG or echocardiographic criteria, was present in 20.2% of the study group; the prevalence of LVH was much higher in the hypertensive subgroup (27.1%) versus normotensive subjects (14.5%) (Figure 2).

The presence of CAD was defined by either one of the following criteria:

- Clinical: history of myocardial infarction / angina pectoris / myocardial revascularization (either by percutaneous coronary intervention or coronary artery bypass graft)
- 12-lead ECG: presence of pathological Q waves or ischemic ST segment – T wave changes
- Echo: LV segmental hypokinesia
- Anti-ischemic treatment: a combination of an antiplatelet agent, a beta-blocker, a statin ± a nitrate in the 2 weeks prior to study enrollment

The diagnostic of CAD was mainly established based on ECG changes and the prevalence of CAD was 25.9% in the study group and 32.1% among the hypertensive subjects (Figure 3). Atrial fibrillation was defined by either documented personal history of atrial fibrillation or by the presence of atrial fibrillation on 12-lead ECG tracings. 5.4% of the whole study population and 8.1% of the hypertensive population had at least one criteria of atrial fibrillation fulfilled (Figure 4). Definition criteria for HF were either documented personal history of HF or a LVEF<50% by Simpson biplane method. 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 ($p<0.0001$). The prevalence of HF in the study group was 9.2%, while the prevalence of HF among the hypertensive subjects was 15.3% (Figure 5).

In fact, when compared with the hypertensive subjects from the previous SEPHAR survey, the hypertensive population in SEPHAR III had a much higher prevalence of asymptomatic cardiac damage (namely, LVH), as well as a higher prevalence of clinically overt cardiac damage, both in terms of

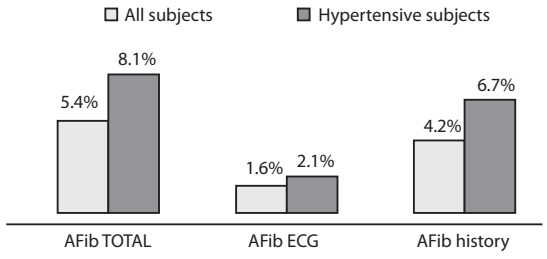

Figure 4. *Prevalence of atrial fibrillation in the SEPHAR III population.*

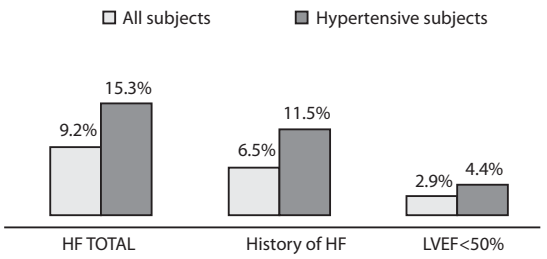

Figure 5. *Prevalence of heart failure in the SEPHAR III population.*

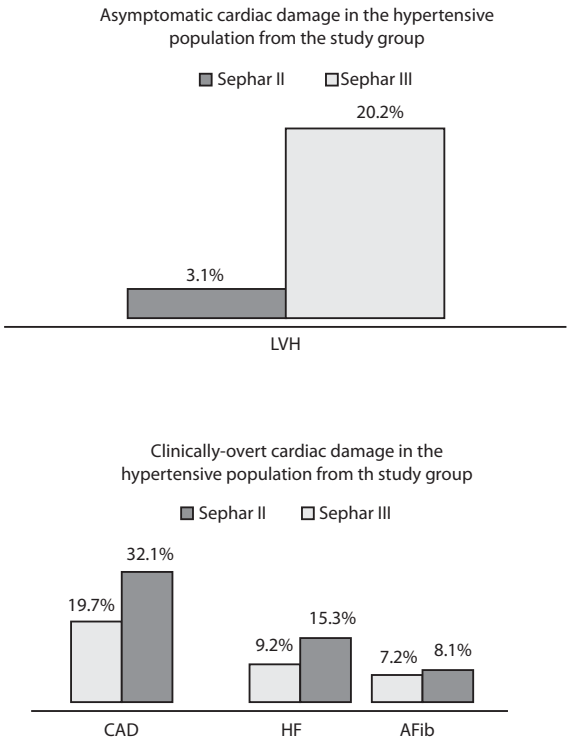

Figure 6. *Upper panel: Prevalence of asymptomatic cardiac damage (left ventricular hypertrophy) in the hypertensive population in SEPHAR III versus SEPHAR II. Lower panel: Prevalence of clinically overt cardiac damage (coronary artery disease, heart failure, atrial fibrillation) in the hypertensive population in SEPHAR III versus SEPHAR II.*

CAD, atrial fibrillation and HF (Figure 6). Our study showed that in Romania, not only is there a high prevalence of HT, but also a high prevalence of cardiac damage among adult hypertensive population.

Conclusion

HT is a main contributor to the global burden of CV disease; hence, early diagnosis and strict BP control are mandatory in order to improve the patients' prognosis. The high prevalence of cardiac damage among hypertensive patients highlights the importance of a thorough evaluation of the hypertensive patient and a therapeutic strategy not only targeting optimal BP control, but also aiming to diminish HT-induced organ damage. Why some hypertensive patients remain asymptomatic, while others progress to subclinical or clinical cardiac damage still remains to be established.

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