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Existence Of Right Ventricular Structural And Functional Changes In Essential Hypertension And Its Importance In Modern Medicine

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Abstract

The structural and functional changes of left and right ventricles as well as the existence of ventricular interaction in patients with arterial hypertenison (AH) were discussed in many research papers. Therefore, published data regarding right ventricular changes under influence of AH are scarce, non-univocal, and sometimes contradictory. Furthermore, there is a significant lack of clinical trials addressing the influence of circadian BP profile on RV structure and function.

The importance of right ventricular function in maintaining global cardiac performance was proven. However, the importance of the right ventricular structure and function for cardiovascular morbidity and mortality is still under debate. Despite the abundance of the study data and high vulnerability of the right ventricle under influence of AH, the world's leading contemporary guidelines of the AH management, right ventricular remodeling, its morphology, function, evaluation, predictive and prognostic value are neither discussed nor mentioned. Hence, we strongly believe that further investigations are needed to determine the exact clinical utility and

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prognostic value of right ventricular functional and morphological changes in patients with arterial hypertension. Moreover, standardization and improvement of diagnostic methodologies of the RV changes via echocardiography, computed tomography, and Magnetic Resonance Imaging are important, which might have a crucial meaning for professionals involved in AH management.

The review article aims to discuss anatomic and physiologic aspects of the right ventricle and their discrepancies according to age, sex, and race, the prognostic meaning of RV remodeling, and review current publications regarding the influence of high blood pressure and its circadian profile on the prevalence of functional and structural changes of RV. Hence, we performed a literature search of the PUBMED database using the medical subject headings "arterial hypertension", "essential hypertension", "systemic hypertension", "circadian BP profile", "remodeling", "right ventricle", "morphology", "anatomy" and "function". A manual search for additional studies was performed using references cited in the original articles.

Keywords: Arterial Hypertension, Right Ventricle, Non-Dipping, Ventricular Interaction, Ventricular Remodeling

Introduction

Over the centuries, researchers paid enormous attention to the evaluation of left ventricle (LV), its geometry, and function in patients with arterial hypertension (AH). AH is the most important cardiovascular risk factor involved in the transition process from normal structure and geometry to LV remodeling by inducing interstitial fibrosis and myocyte hypertrophy resulting in alterations of both LV systole and diastole (Frohlich et al., 2011; Treibel et al., 2017; Altemani, 2016). LV hypertrophy nowadays is considered as the pivotal biomarker of hypertension-mediated subclinical organ damage and an intermediate step from hypertension to heart failure (Messerli et al., 2017). It is proven that LV hypertrophy is a predictor of cardiovascular events and indicates increased CV risk (Antikainen et al., 2016; Williams et al., 2018; Volpe et al., 2012; de Simone et al., 2015). Hence, normal values of LV dimensions, mass variabilities, functional characteristics, and volumes are well established.

Historically, scientists considered the right ventricle (RV) as a hemodynamically unimportant heart chamber and perceived it as the „low-pressure bystander“ of the left ventricle (Sanz et al., 2019). Accordingly, its clinical meaning and significance have been underestimated. Sir William Harvey was the first who described the importance of structural and functional changes of RV in his treatise “De Motu Cordis” in 1616 year.

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Left ventricular hypertrophy (LVH) is an important marker of hypertension-mediated organ damage and an intermediate step from hypertension to heart failure. Until the first half of the 20th century, studies regarding RV were overshadowed and the hypothesis that human circulation could function adequately without contractility of RV was prevalent among scientists (Haddad et al., 2008). Due to the underestimation of RV meaning and its complex shape, assessment of RV size, function and geometry was lacking for centuries. Starr et al. in 1943 reported that destruction of RV free wall in dogs did not affect overall cardiac performance (Starr et al., 1943). Angiographic studies performed by Gentzler et al. in 1974 also failed to demonstrate a relationship between right ventricular afterload or peak systolic pressure and pump performance (Gentzler et al., 1974). Right heart, as a scientific target, became relatively more important from 1950 to the late 1970s. The RV was "rediscovered" only after the development of cardiac imaging techniques due to evidence indicating that the RV can indeed be a significant contributor to functional hemodynamics and cardiac output (Guimaron et al., 2018; Konstam et al., 2018). RV function was found to have a vital role in cardiovascular and total morbidity and mortality (Carluccio et al., 2018; Naksuk et al., 2018; Murninkas et al., 2014). It is well-established fact that a decrease in RV systolic function is an independent predictor of adverse outcomes, including heart failure-associated hospitalization and mortality (Sanders et al., 2020). Studies showed, that pathologies involving pulmonary or systemic circulation, such as arterial hypertension, heart failure, vascular heart disease, mitral and aortic valve diseases, shock, sepsis, etc. are in association with changes in RV function and geometry (Akintunde et al., 2010; Tadic et al., 2018; Monitillo et al., 2020; Rallidis et al., 2014; Ye et al., 2014; Winkelhorst et al., 2020; Lanspa et al., 2021). Therefore, published data regarding right ventricular changes under influence of AH are scarce, insufficient, heterogeneous, and sometimes contradictory. Furthermore, there is a significant lack of clinical trials addressing the influence of circadian BP profile on RV structure and function.

The basics of RV dimensions and function were partly and quite superficially described in the recommendations for chamber quantification published in 2005 by the American and European Societies of Echocardiography, which mainly focused on the left heart assessment (Lang et al., 2005). Relatively complete recommendations regarding RV assessment were published in 2010 in the "Guidelines for the Echocardiographic Assessment of the Right Heart in Adults" (Rudski et al., 2010). Hence, because of the importance of RV function for prognosis, there is a need for further improvement of diagnostic methodology as well as standardization of the RV echocardiographic, computed tomography, and magnetic resonance imaging findings.

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This review article aims to discuss anatomic and physiologic aspects of right ventricle, the influence of age, sex, and race on these parameters, prognostic meaning of RV remodeling and to provide an overview of current knowledge regarding the influence of high blood pressure and its circadian profile on the prevalence of functional and structural changes of RV. Hence, we performed a literature search of the PUBMED database using the medical subject headings "arterial hypertension", "essential hypertension", "systemic hypertension", "circadian BP profile", "remodeling", "right ventricle", "morphology", "anatomy" and "function". A manual search for additional studies was performed using references cited in the original articles.

Main Text

Anatomic Aspects of RV

The RV and LV have different embryological origins. The RV originates from the secondary heart field and LV from the primary heart field; hence, in the healthy heart, RV has a specific structure that differs from LV (Friedberg et al., 2014). Transverse fibers are predominantly located in the RV free wall that surrounds the septum, whereas the septum contains oblique helical fibers without a transverse component. RV is located behind the sternum and anterior to LV. It forms the majority of the anterior, as well as the inferior border of the cardiac silhouette. In comparison with LV, in a healthy adult RV is a thin-walled structure, which is well accustomed to low pulmonary resistance and low afterload (Chakane, 2020; Taverne et al., 2020). Unlike the LV, which has an ellipsoid or conical shape, the RV has a unique triangular (in lateral section) and crescent (in cross-section) or pyramidal shape that wraps around LV. The RV has one-sixth of the muscle mass of LV as it pumps against approximately one-sixth of the resistance of the LV encounters. However, the RV pumps equal cardiac output as LV (Friedberg et al., 2014).

Unlike the LV, RV does not have a helicoid shape. The interventricular septum represents a dominant biventricular helical structure that determines the systolic function of both ventricles and is considered as the "lion of the RV function" (Tadic et al., 2018; Buckberg et al., 2006; Buckberg et al., 2014). The RV and LV are closely interrelated not only through the septum but also shared epicardial circumferential myocytes and the pericardial space, all of which constitute the anatomic basis for biventricular functional systolic and diastolic interdependence (Naeije et al., 2017; Sanz et al., 2019).

In 1975, Goor and Lillehei defined three components of the RV; namely, (1) the inlet, which consists of the tricuspid valve, chordae tendineae, and papillary muscles; (2) the trabeculated apical myocardium; and (3) the infundibulum, or conus, which corresponds to the smooth myocardial outflow

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region. Thus, a three-part description of RV was adopted and still is used in clinical anatomy (Muresian et al., 2016).

RV has a complex shape and is composed of multiple muscle layers that form a 3-dimensional network of fibers. The RV wall is about 2–5mm in thickness, 25±5g/m2 in weight, and mainly composed of superficial and deep muscle layers (Wang et al., 2019). Muscular fibers of the superficial layer of the RV are mainly arranged circumferentially and the deep muscle fibers are longitudinally aligned base to apex. Mitral and aortic valves are in a fibrous continuity in the left ventricle, while tricuspid and pulmonary valves are separated from each other by the ventriculoinfundibular fold, which is the unique characteristic feature of the RV (Ho et al., 2006; Saremi et al., 2013; Addetia et al., 2014).

The position of the interventricular septum influences the shape of the RV. It is considered that the septal motion has a contribution to left and right ventricular function and is a major determinant of overall RV performance (Lindqvist et al., 2006; Klima et al., 1998; Buckberg et al., 2014).

The evaluation of the RV structure is dependent on the assessment of RV wall thickness. In the global population free of cardiovascular disease, RV wall thickness can be considered as an important predictor of morbidity and mortality (Kawut et al., 2012). In comparison with conventional echocardiography, three-dimensional echocardiography and speckle tracking imaging give better insight for the assessment of RV morphology, function, and mechanics (Tadic, 2015). Technological advances have made it possible to visualize and characterize a variety of diseases that affect the RV more precisely. According to Goetschalckx et al., MRI imaging of the RV is patient-tailored, integrating RV functional and volumetric analysis, which gives an excellent opportunity for assessment of cardiac morphology, myocardial tissue characteristics, great vessel anatomy, and flow patterns, which provide the clinician a complete view of the RV being an essential part of the cardiopulmonary system (Goetschalckx et al., 2010). A meta-analysis conducted by Kim et al. demonstrated a good agreement and very strong correlations between RV anatomical and functional parameters on CT and cardiac MRI (Kim et al., 2020). For today, cardiac MRI is considered as the reference standard; however, the technique is contraindicated in some patients, such as those with implantable or supporting devices and claustrophobia. Therefore, CT can be considered as an alternative tool for cardiac chamber function evaluation in patients who cannot undergo cardiac MRI (Rizvi et al., 2015; Gopalan et al., 2011). Hence, cardiac MRI and cardiac computer tomography are the most accurate methods, but their availability and high cost remain the major limitation to their routine use in everyday clinical practice (Galea et al., 2013; Mak et al., 2020).

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Physiological Aspects of Right Ventricular Function

The heart is the first organ to be formed during embryogenesis, which starts beating on day 21. Heart formation consists of four key phases: tubular heart formation, cardiac looping, chamber formation, and complete septation with the development of the coronary arteries (Taverne et al., 2020).

The importance of RV function is evident even during the intrauterine period, when it serves as the predominant ventricle and shares a similar preload and afterload with the LV but ejects approximately 66% of the cardiac output. At this stage of development, blood flow per gram of myocardium is identical in both ventricles (Mielke et al., 2001). With the closure of the foramen ovale and the ductus arteriosus, which occur at birth, pulmonary vascular resistance decreases, which is accompanied by a reduction in RV pressure and coronary blood flow, with a concomitant increase in LV myocardial blood flow (Walker et al., 2013). Consequently, functional capacities of both ventricles dramatically change after birth and the LV quickly develops into a thick-walled, highly contractile chamber, while the RV becomes a highly compliant, thin-walled, and poorly contractile chamber (Hooper et al., 2015).

The blood supply of RV is mainly derived from the right coronary artery (RCA) and partially from the left anterior descending branch of the left coronary artery (LCA). The timing of RCA blood flow is unique. Unlike the blood flow in LCA, in RCA blood flows during diastole and systole. This "dual source" of RV coronary blood flow can be considered as a reason for the relatively small percentage of significant RV dysfunction in patients with significant occlusion of the RCA (Haddad et al., 2008).

The RV has a unique and highly synchronized fashion of contraction. RV sinus and apex contract 20 to 50 ms earlier than the conus, resulting in a peristalsis-like motion (Calcutteea et al., 2011). Because of higher curvature, late contraction, and greater inotropic response, the conus may serve as a buffer against high systolic pressure (Hadad et al., 2008). In contrast with the vortex-dominated flow organization of the LV, RV is mainly characterized by the helical flow along the septum, largely circumventing the apex (Sengupta et al., 2013). Accordingly, the role of the apex may be maintaining a smooth and continuous blood flow rather than contributing to ejection (Fredriksson et al., 2011).

Although traditionally it has been usual to consider the function of the left and right ventricle in isolation, experimental studies confirmed interactions between the two sides of the heart; namely, the importance of LV in RV performance. LV contraction generates 20% to 40% of RV stroke volume, which is largely mediated by septal contraction (Lahm et al., 2018; Penny et al., 2016). In contrast with the LV, RV has a significantly thinner wall and lower volume-to-wall-surface area ratio, which makes RV unable to

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cope with brisk increments in pulmonary artery pressures. Hence, an acute increase of preload and/or afterload is immediately associated with "heterometric" adaptation revealed as RV dilatation, which after several minutes is replaced by an "homeometric" adaptation and increased contractility (Sanz et al., 2019)

The functional status of RV is influenced by intrinsic factors that determine RV contractile performance such as the contractile state of the RV myocardium and by extrinsic factors, which determine RV pump performance such are afterload, preload, right coronary artery perfusion pressure, contractile state of the interventricular septum, left ventricular performance, constraining effects of the pericardium and intrapericardiac pressure.

Age, Sex and Race Differences in Right Ventricular Structure and Function

It is a well-known fact that LV mass and volumes vary significantly by age, sex, and race (Natori et al., 2006; Cheng et al., 2009). Because of substantial differences between morphology, physiology, workload, and perfusion of left and right ventricles, extrapolation of findings from the LV to the RV is practically impossible.

Results from studies, investigating relationships between older age and LV mass are controversial. They showed increased, decreased, or not changed LV mass with aging (Sandstede et al., 2000; Tamborini et al., 2010; Ventetuolo et al., 2011; Ventetuolo et al., 2016). The Multi-Ethnic Study of Atherosclerosis (MESA), where were involved 4123 patients (mean age 61.5±10.1 years old) showed a strong association between age, sex, race, and RV mass, volumes, and ejection fraction (EF) (Kawut et al., 2011). Similar to the MESA study, other authors also revealed a strong association between older age and lower RV mass and higher RV EF (Sandstede et al., 2000; Maceira et al., 2006). Autopsy studies confirmed the existence of "aging cardiomyopathy", which is characterized by myocyte loss and change in myocyte quality, which explains the age-related decrease of RV mass and increased RV EF (Olivetti et al., 1995). In contrast with the above data, results obtained by Hudsmith et al. show that men and women older than 35 years old have higher RV mass in comparison to those, who are younger than 35 years old (Hudsmith et al., 2005). Maffessanti et al., as well as Sandstede et al., reported sex-specific differences in RV mass and volume; RV volumes were larger and EF lower in men than in women; hence, sex was a significant determinant of RV size even after scaling for anthropometric variables (Maffessanti et al., 2013; Sandstede et al., 2000). Similar results were obtained by Kawut and Tamborini, who also reported lower RV EF in male patients compared to females (Kawut et al., 2011; Tamborini et al., 2010).

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These findings may be explained via hormonal influences. The MESA-Right Ventricle Study showed a strong association between higher estradiol levels and better systolic function of RV as well as higher androgen levels and greater RV mass and volumes in both sexes (Ventetuolo et al., 2011). Sex-based differences in right heart function were explained as alterations in estradiol metabolism in women and testosterone-androgen receptor interactions in men, where race appears to be an important modifier of some of these relationships (Ventetuolo et al., 2016). Compared with whites, blacks and Chinese Americans have lower and Hispanics higher RV mass (Kawut et al., 2011). Unlikely to RV mass, blacks have greater LV mass, and accordingly, LV hypertrophy is frequently found in normotensive as well as in hypertensive subjects (Drazner et al., 2005; Rodriguez et al., 2010; Katholi et al., 2011). Therefore, Asch et all. found out that in contrast with Asians and Mexicans who have smaller heart dimensions and volumes, people of White and Black race have similar heart dimensions and volumes (Asch et al., 2019).

In a Bogalusa Heart Study and CDAH Study was revealed that childhood adiposity and different body growth patterns have strong effects on interracial differences of left and right ventricle mass and cardiac structure (Li et al., 2004; Tapp et al., 2014).

Influence of arterial hypertension on RV structure and function

The crucial role of the renin-angiotensin system (RAS) in the regulation and stabilization of BP, extracellular fluid volume homeostasis, and consequently in the pathogenesis of AH has been proven decades ago. Angiotensin II is one of the most powerful vasoconstrictors, which contributes to the development of end-organ damage through direct effects on cardiac, vascular, and renal tissues. It influences the adrenals, adipose tissue, nervous system, digestive organs, skin, reproductive tract, and sensory organs (Te Riet et al., 2015). RAS's role on LV structure and function is established, but data regarding its contribution to RV performance are heterogeneous (Ikram et al., 1982; Therrien et al., 2008). Interventions targeting RAS to prevent RV remodeling in the setting of pulmonary hypertension showed promising results (Okada et al., 2009). Ventetuolo et al. studied the influence of RAS blockage on RV structure and function via cardiac magnetic resonance imaging in 6814 patients without clinically manifested cardiovascular diseases and revealed a strong association between RAS blockage and RV mass and volume in a race-specific and LV-independent manner (Ventetuolo et al., 2012).

The absolute majority of the studies regarding AH focused on LV assessment; because of chronic pressure overload while AH, formation of LV hypertrophy maintains normal LV systolic function (Katholi et al., 2011; Angeli et al., 2015). Studies regarding RV are mostly performed in patients with lung diseases. These studies revealed that RV hypertrophy and diastolic

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dysfunction is a common finding due to the alveolar hypoxia in patients with chronic obstructive pulmonary disease and obstructive sleep apnoea syndrome (Maripov et al., 2017; Raisinghani et al., 2015; Güvenç et al., 2013; Jatav et al., 2017). RV performance in patients with AH is not well established yet, because of lacking evidence-based data.

French physician and neurologist Hippolyte Bernheim (1840-1919) was the first, who described interventricular septum hypertrophy due to AH and consequent RV changes. He described 10 cases in his original article and titled it "Venous asystole in hypertrophy of the left heart with associated stenosis of the right ventricle." In that article, Bernheim included two drawings, one of a normal heart and one with a thickened left ventricular wall with the thick ventricular septum protruding toward the right ventricular cavity (Chung et al., 2013). Bernheim's syndrome has been a topic of discussion for over a century. It has been reported to be caused by AH and aortic stenosis due to the severe rightward movement of the hypertrophied ventricular septum resulting in compression of the RV cavity leading to right-sided heart failure without pulmonary congestion. In 1936, Podestia renamed Bernheim's syndrome and called it dextroventricular stenosis (East et al., 1949). Olivary et al. revealed that the development of ECG signs of LV strain is related to the abnormal performance of both sides of the heart and suggested the hypothesis of a functional interdependence of the two ventricles (Olivari et al., 1978). Iliev et al. studied the development of cardiac hypertrophy initiated by systemic hypertension in different age groups of spontaneously hypertensive rats. In both ventricles, authors described focal myocytolysis, cardiomyocytic hypertrophy, and increased collagen deposition in the interstitial space. Changes were present in the cardiomyocytic nuclei, the development, and maturity of the intercalated discs, the arrangement, maturity, and organization of the myofibrils, the ultrastructure and localization of the mitochondria, as well as changes in the components of the interstitium. Researchers demonstrated the involvement of the right ventricle and the development of cardiac hypertrophy in response to systemic hypertension in both ventricles (Iliev et al., 2019). Other scientists also revealed AH-mediated changes in RV (Alpert et al., 1985; Ferlinz, 1980; Nunez et al., 1987).

The existence and importance of RV dysfunction in patients with AH were widely recognized in recent years, with the development of new imaging modalities (Marketou et al., 2019). However, very little is known about the nature of RV performance when the left ventricle is exposed to a chronic pressure overload that takes place in essential hypertension (Abdeltawab et al., 2018). The usage of fractional area shortening, tricuspid annular plane systolic excursion (TAPSE), or tissue Doppler parameters (systolic peak velocity of the RV free wall at the level of the tricuspid valve and isovolumetric contraction time) for assessment RV function in hypertensive patients resulted

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in controversial results (Hanboly, 2016; Gregori et al., 2014; Tumuklu et al., 2007; Karaye et al., 2012). Hence, using of myocardial performance index (Tei index) as a parameter of RV dysfunction, the negative influence of AH on RV systolic-global function becomes evident (Gregori et al., 2014). Unlike the uncertainty that exists in the relationship between AH and RV systolic function, almost all investigators agree that AH impacts RV diastolic function (Tadic et al., 2014; Tadic et al., 2015; Tadic et al., 2017). In contrast with RV systolic function, the evaluation of RV diastolic function is mainly performed by pulsed and/or tissue Doppler indices. Myslinski et al. studied RV structure and diastolic function in 59 patients with untreated, mild to moderate AH to establish the possible mechanisms of RV dysfunction in hypertensive patients (Myslinski et al., 1998). In comparison with Gottdiener et al. who found that the average RV wall thickness in healthy subjects is 4 ±1mm (range 3–5 mm) measured from the parasternal window, Myslinski et al. revealed an increased RV wall thickness till the upper limit (7mm), significantly thicker interventricular septum and posterior wall, lower RV diastolic filling time and higher peak atrial velocity in hypertensive individuals (Gottdiener et al., 1985). Similar results were obtained by Nunez et al., who demonstrated RV wall hypertrophy in hypertensive subjects and a positive correlation between the thickness of the left and right ventricles, which can suggest the similar influence of AH on both ventricles (Nunez et al., 1987).

Significant correlations between left and right ventricular diastolic filling parameters in hypertensive subjects were demonstrated by Habib et al and Chakko et al. (Habib et al., 1992; Chakko et al., 1990). In comparison with normotensive subjects, hypertensive counterparts have significantly higher RV wall thickness, right atrial volume index, and tricuspid E/e' ratio, lower RV ejection fraction, increased pulmonary artery pressure, and pulmonary arteriolar resistance (Olivari et al., 1978; Ferlinz, 1980; Tadic et al., 2018). Abdeltawab et al. demonstrated that RV diastolic dysfunction is not only an early marker that is correlated to the presence of systemic arterial hypertension but also showed it to be a marker of its severity and degree of hypertension (Abdeltawab et al., 2018)

The impairment of RV systolic function in AH could be explained via RV hypertrophy, increased RV filling pressures, and ventricular interaction. Therefore, RV diastolic dysfunction might be explained by increased stiffness of the RV caused by hypertrophy, ventricular interaction, the retrograde transmission of increased LV filling pressure to the pulmonary circulation and ultimately to the RV, negative influence of renin-angiotensin-aldosterone and sympathetic nervous system on pulmonary circulation (Ferlinz, 1980).

Fiorentini et al. found a strong positive correlation between systemic vascular and pulmonary arteriolar resistance and suggested, that systemic, as well as pulmonary vasculature, are influenced by the same type of

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dysregulation factors in systemic AH (Fiorentini et al., 1985). Cicala et al. via pulsed tissue Doppler revealed the main role of ventricular interaction in the formation of changes in right ventricular wall compliance (Cicala et al., 2002). The fact that development of increased right ventricular wall thickness takes part side by side with left ventricular hypertrophy points out on a presence of not only structural (RV and LV have common myocardial fibers, share the ventricular septum, and are enclosed within the pericardium), but functional interventricular interaction and interdependence as well (Hanboly, 2016). Todiere et al. confirmed that the unstressed ventricle is not immune to the effects of systemic hypertension; namely, systemic hypertension is associated with concentric right ventricular remodeling and impaired diastolic function. Structural and functional right ventricular adaptation to systemic hypertension tends to parallel the homologous modifications induced by a systemic hemodynamic overload on the left ventricle (Todiere et al., 2011). Results of the studies discussed above demonstrate the involvement of the right ventricle in AH and the relationship between the left and right ventricular function, despite the exact mechanisms of RV hypertrophy in AH are not clear. There are three major mechanisms, that could explain RV hypertrophy in AH. First, overstimulation of the sympathetic system and the renin-angiotensin-aldosterone system, which is the cornerstone for hypertension pathogenesis and could be responsible for increased pulmonary arteriolar resistance and, RV hypertrophy (Schermuly et al., 2011). Second, the mechanical interaction between the right and left ventricles through the interventricular septum and third, oxidative stress and endothelial dysfunction could induce changes in pulmonary circulation leading to RV hypertrophy (Tadic et al., 2018).

RV wall and interventricular septum thickening may play an important role in RV diastolic dysfunction in patients with AH. A lower than normal RV ejection fraction in hypertensive patients might be indicating the impairment of RV contractility. Thus, we can suggest that the assessment of RV performance in patients with AH, may be an additional, sensitive indicator of the course of disease (Vriz et al., 2018).

Relationship between circadian BP profile and RV function and morphology in hypertensive patients

Circadian BP rhythm and its pattern is the result of cyclic day-night alterations in behavior (physical activity, mental stress, environmental phenomena, posture) and endogenous circadian rhythms (neural, endocrine, endothelial, hemodynamic variables). The prognostic meaning of circadian BP profile for hypertensive patients is well documented (Verdecchia, 2000; Tsioufis et al., 2011). Studies that accounted for daytime and night-time BP in the same statistical model found that night-time BP is a stronger predictor of outcomes than daytime BP (Parati et al., 2014).

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Historically, studies mostly addressed left ventricular changes in hypertensive patients with different circadian BP profiles (Yi et al., 2014; Cuspidi et al., 2013; Mezue et al., 2016; Abdalla et al., 2017). Tadic M. et al. were the first who studied RV mechanics and function in untreated hypertensive patients with different circadian BP patterns (Tadic et al., 2012; Tadic et al., 2014). They revealed that a non-dipper BP profile represents one of the independent predictors of RV diastolic and global function. Non-dipper hypertensive patients, in comparison with dippers, have significantly impaired RV function and mechanics, increased RV volumes, and decreased ejection fraction. After a few years they proved that RV mechanics are worse in the night-time and daytime-night-time hypertensive patients than in normotensive controls and isolated daytime hypertensive patients (Tadic et al., 2018). Akçay S. et al. evaluated right ventricular function in 131 hypertensive patients and similar to previous results revealed that non-dipper hypertensive patients compared to patients with dipper circadian BP profile have more deteriorated RV function (Akçay et al., 2013). Erturk M. et al. demonstrated that non-dipper hypertensives have increased left and right ventricular subclinical systolic dysfunction compared with dippers (Erturk et al., 2014). Ivanovic B. et al. in the cross-sectional study, which included 376 hypertensive patients, found out that RV thickness and most RV diastolic parameters significantly and progressively worsened from the dippers, over the non-dippers and the reverse dippers (Ivanovic et al., 2013). In their study nighttime systolic BP, nocturnal systolic BP fall, and the non-dipping profile were independently associated with LV and RV structure, as well as with diastolic function.

Tadic et al. conducted a prospective study and investigated the predictive value of RV remodeling and 24-h BP patterns on long-term cardiovascular prognosis in the initially untreated hypertensive patients. They included 505 patients and followed for a median period of 9 years. Authors revealed that LV hypertrophy, night-time SBP, the non-dipping BP pattern, right atrial enlargement, RV hypertrophy, RV diastolic dysfunction, and RV systolic dysfunction were associated with adverse cardiovascular events. Moreover, RV hypertrophy and the reverse dipping BP pattern were independent long-term predictors of the cardiovascular outcome (Tadic et al., 2020). Moreover, in comparison with patients with physiological night-time BP lowering i.e. dipper circadian BP profile (nighttime BP drop is 10-20%), non-dipper hypertensive patients who do not have night-time dipping (nighttime BP drop is <10%) or have higher night-time BP than daytime (reverse dippers), have a substantially increased risk of cardiovascular and cerebrovascular morbidity and mortality (Mancia et al., 2015; Hansen et al., 2011; Hermida et al., 2011; Yano et al., 2012).

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Conclusion

Clinical studies indicate that RV hypertrophy and dysfunction are common in patients with AH. Despite proven interaction between the left and right ventricles while AH, there is still debate on the prognostic value of RV function and its association with clinical outcomes (Cuspidi et al., 2013; Bleasdale et al., 2002; Peyrou et al., 2017). Published data regarding right ventricular changes under influence of AH are scarce, non-univocal, and sometimes contradictory. Furthermore, view clinical trials addressing the influence of circadian BP profile on RV structure and function. There is not homogenous and univocal data regarding assessment methodology and principles of RV. Hence, the term "right heart", its remodeling, assessment, and prognostic meaning are not discussed, even mentioned in the world-leading contemporary guidelines of the AH management (Whelton et al., 2018; Gabb et al., 2016; Nerenberg et al., 2018; Williams et al., 2018; Umemura et al., 2019). Consequently, further investigations are needed to determine the clinical utility and prognostic value of RV functional and morphological changes in patients with AH. It is immensely important to standardize and improve the diagnostic methodology of RV evaluation via echocardiography, computed tomography, and/or magnetic resonance imaging, which might have a crucial meaning for professionals involved in hypertension management to improve patients' prognosis.

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