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Review

Blood Pressure Variability in Hypertension a Rehabilitation Perspective

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Abstract

The role of blood pressure variability (BPV) as an important marker of cardiovascular (CV) health, specifically its relationship with arterial stiffness and left ventricular remodelling in patients with hypertension. This review with the aim of elucidating the intricate relationship between BPV, arterial stiffness, and cardiac remodeling has been performed. BPV as both a risk factor and a target of treatment has also been evaluated. Results indicate that BPV is involved with a pivotal contribution to cardiovascular events with an independent contribution towards arterial stiffness and with adverse left ventricular remodelling. The article concludes that BPV is a modifiable risk factor and that there is a need for an intervention in specific regions. BPV is a part of the therapy target that is significant in the treatment of hypertension. Optimisation of risk and prevention need a multi-disciplinary approach involving rehabilitation therapy and lifestyle modification in optimising cardiovascular condition and patient's outcomes.

Keywords: blood pressure variability; hypertension; rehabilitation

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1. Introduction

Blood pressure variability (BPV) is the definition of variations in BP over various time intervals like beat-to-beat over a day over a few days and from clinic visit to clinic visit [1,2]. Unlike the traditional mean blood pressure, BPV quantifies dynamic blood pressure variability which may express features of underlying cardiovascular dysregulation. In hypertension increased BPV has been associated with adverse cardiovascular outcomes independent of mean blood pressure levels [3]. Additionally, for any 25hrs average BP target organ damage can be severe in patient with Higher BP variability. Higher BPV in hypertensive patients has been linked to a higher risk of stroke, coronary heart disease and mortality highlighting its prognostic significance regardless of static BP levels [4].

Physiological substrate of BPV is multifactorial and includes interaction between neural, humoral, and mechanical mechanisms that influence vascular tone and cardiac output. Such dynamic variability can cause vascular remodeling, endothelial dysfunction, and myocardial stress and result in structural and functional changes in the heart and vasculature. Identification of early markers of cardiovascular impairment in patients with essential hypertension and high BPV can result in risk stratification and intervention [2,3].

In the cardiovascular system, left ventricle and arterial wall stiffness are critical to cardiac performance and vascular health. Left ventricular stiffness is a diseased state in which the heart muscle particularly the left ventricle is less compliant and its role to fill with blood during diastole is impaired [5]. Similarly, arterial stiffness reflects the rigidity of large arteries that occurs when the elastic function of the arterial wall is compromised more frequently due to aging or chronic hypertension [6]. Increased arterial stiffness is a marker of vascular aging and a predictor of cardiovascular events like myocardial infarction and stroke [7]. Current evidence suggests a

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connection between BPV, and left ventricular and arterial stiffness in which BP variability may be implicated in vasculature and heart structural and functional changes [8]. However, the precise mechanisms through which BPV is connected with these measures of stiffness are not yet understood. Consequently, the objective of the present review is to find and synthesize current evidence for BPV association with left ventricular and arterial stiffness in hypertensive patients. Exploration of such interactions would provide some insights into the role of BPV in the cardiovascular stiffness pathophysiology and hypothesize its potential utility on hypertension treatment and prognosis.

2. Types of Blood Pressure Variability

BPV refers to the fluctuation of BP over different time intervals. BPV provides information in addition to mean blood pressure readings that capture dynamic change that can affect cardiovascular health. BPV is typically classified into different types based on the time interval over which the fluctuation takes place each having distinct implication for cardiovascular outcomes [9,10]. Short-term BPV is beat-to-beat and day-to-day variability like that of 24-hour variation. Physical activity, stress, and diurnal rhythms may cause this variation. Short-term BPV is typically measured with the help of ABPM and is associated with cardiovascular morbidity, especially where there is great variability [11]. Long-term BPV encompasses variations lasting weeks, months, or years. Variations can be quantified by comparing clinic BP levels or using multiple ABPM performed over long periods. Long-term BPV estimates an individual's global BP control stability and increased long-term BPV has been linked to increased risk of stroke, coronary events, and all-cause mortality [4]. Visit-to-visit BPV This type of BPV is defined by variation in BP levels between consecutive clinical visits. Visit-to-visit BPV is influenced by disease severity, clinical conditions, and medication adherence. Studies have shown that increased visit-to-visit BPV is an independent and unique predictor of cardiovascular morbidity and mortality [12]. The variability has been seen to be prominently noted in the elderly and those with pre-existing cardiovascular disease [13–15].

3. Mechanisms Affecting Blood Pressure Variability

BPV is caused by complex mechanisms that involve the nervous system, endocrine regulation, and vascular responsiveness. the autonomic nervous system plays a prime role in regulation of blood pressure variability particularly due to interaction among sympathetic and parasympathetic activity. The sympathetic nervous system reacts towards stress and stimuli to create acute increases in BP. Sympathetic overactivation commonly present in hypertensive patients is one of the causes of increased BP variability and could ultimately lead to target organ damage [11,16–19]. Adrenaline, cortisol, and angiotensin II are a few of the hormones that play roles in regulating BP and thus BPV. The renin-angiotensin-aldosterone system (RAAS), for example, regulates BP through vascular tone control and sodium retention. Dysregulation of such hormonal systems common in hypertensive patients might increase BPV [20–22]. In addition, cortisols circadian rhythm is responsible for daily variations in BP that affect early-morning BP peaks. Vascular Mechanisms: arterial stiffness and endothelial function are the major vascular determinants of BPV. Stiffer arteries have reduced buffering capacity for pressure changes resulting in increased BP fluctuations. Endothelial dysfunction most often due to inflammation or oxidative stress can result in damage to vasodilation further destabilizing blood pressure regulation [23].

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4. Impact of Blood Pressure Variability on Cardiovascular Structure and Function

4.1. Effects on Cardiac and Arterial Structures

Increased BPV has been associated with harmful alterations in cardiac as well as arterial morphology. BPV increase can potentially lead to endothelial dysfunction preceding atherosclerosis by causing intermittent shear stress on vascular endothelium. This tension damages endothelial cell function to cause inflammation and plaque formation contributing to arterial stiffness and reduced compliance [5,8,23,24]. This stiffness of the arteries, in turn, enhances heart workload since the heart must pump against elevated resistance, with the potential to cause left ventricular hypertrophy (LVH) and remodeling.

4.2. Role in Left Ventricular Hypertrophy and Remodeling

BPV contributes to LVH and remodeling through numerous mechanisms. Repeated pressure overload due to variability of BP brings about growth of the myocardial cells and fibrosis, contributing to increased left ventricular mass and altered geometry [25,26]. Such remodeling can lead to compromised diastolic function and reduced cardiac efficiency. Studies have proven that greater BPV is independently associated with greater left ventricular mass and greater concentration of concentric hypertrophy when adjusting for mean blood pressure levels [27]. This proves that BPV independently contributes to cardiac structural remodeling apart from its effect of chronic hypertension.

5. Left Ventricular Stiffness and Blood Pressure Variability

BPV has been found to be independently associated with reduced left ventricular compliance. In both hypertensive and normotensive individuals, the relation between increased BPV and impaired relaxation of the myocardium and stiff left ventricle has been noted. For instance, from studies, patients with higher BPV have higher diastolic dysfunction as represented by echocardiographic findings like increased E/e′ ratio and left atrial volume being indicators of left ventricular stiffness and filling pressures [28]. In animal models, BP fluctuations induced in them lead to progressive stiffening of the ventricles to support that it is BPV itself, other than the average BP, responsible for left ventricular compliance changes.

6. Mechanisms Linking BPV to Left Ventricular Hypertrophy

Intermittent Pressure Overload; Repeated BP surges subject the heart to a variable load that triggers compensatory hypertrophy to manage the intermittent stress. The pressure surges deliver a stimulus for myocardial expansion and collagen deposition that increase left ventricular mass and reduce compliance over time [29–31]. Myocardial Fibrosis, BPV is also associated with increased myocardial fibrosis a process with excessive deposition of collagen within the myocardium that interferes with elasticity [32]. Such fibrosis is in part mediated through activation of RAAS during episodes of increased BP favoring synthesis and deposition of collagen [33]. Sympathetic Activation; BPV is often followed by heightened sympathetic nervous system activity particularly in response to stressors. Sympathetic activation causes cardiomyocyte hypertrophy and can exacerbate the fibrotic response of the myocardium with additional stiffening and dysfunction. Oxidative Stress and Inflammation; BP variability can cause oxidative stress which participates in the remodeling process. Oxidative stress incites pro-inflammatory pathways that further amplify fibrosis and structural remodeling in the myocardium. This adds to left ventricular stiffening compounding the adverse effects of BPV on cardiac function [34,35].

7. Arterial Stiffness and Blood Pressure Variability

Arterial stiffness is the reduced arterial elasticity that compromises the ability of arteries to dilate and constrict in response to alterations in pressure during the cardiac cycle. It is a marker of vascular aging and an independent predictor of cardiovascular events [8]. The most frequent method of the assessment of arterial stiffness is the measurement of pulse wave velocity (PWV). PWV measures the speed at which pressure waves travel in the arterial tree with higher values indicating more rigid arteries. Carotid-femoral PWV has become the gold standard of central arterial stiffness and has been shown to have strong predictive value for cardiovascular events and mortality [36,37].

8. Arterial Elasticity and Vascular Aging

BPV includes variation in BP over different time intervals such as beat-to-beat within a day and visit-to-visit. Arterial stiffening and vascular aging have been associated with greater BPV. Repeated BP fluctuations place mechanical stress on the arterial wall that could lead to endothelial dysfunction inflammation and structural alterations such as increased collagen accumulation and elastin degradation. These changes reduce arterial compliance and accelerate arterial stiffening and result in vascular aging [38,39].

9. Clinical Studies Correlating BPV and Arterial Stiffness

A few research works presented a relationship between BPV and arterial stiffness: A study pointed out that higher BPV from visit to visit was associated with higher arterial stiffness measured by PWV in hypertensive patients [24]. There was a relationship between short-term BPV determined by 24-hour ambulatory monitoring and arterial stiffness parameters demonstrating that even short-term variability can negatively affect vascular health [40–43]. A study concluded that greater BPV is linked with greater arterial stiffness and greater cardiovascular risk, implicating a promising clinical usefulness of BPV control in slowing vascular aging [38].

10. Clinical Implications in Hypertension Management

BPV is emerging as an important factor in the management of hypertension because it has been more and more widely recognized as an independent predictor of cardiovascular morbidity and mortality. BPV factors may affect the treatment strategy in hypertensive patients, especially those at high risk of arterial and ventricular stiffness-related complications. While the traditional approach to treating hypertension is to decrease mean blood pressure, BPV also provides additional information regarding a patient's cardiovascular risk. Reducing BPV has been established as equally valuable as decreasing mean blood pressure to minimize adverse effects [4]. The treatment can then be optimized not just to lower total blood pressure but also to normalize BP variability.

Certain antihypertensive medications like ACE inhibitors and calcium channel blockers have been proved to decrease BPV considerably. For instance, the calcium channel blocker amlodipine in once-daily dosage has been proved to decrease BPV more than any other antihypertensive drug class and is particularly helpful in patients with increased BPV. Similarly, ARBs like losartan have been linked to improved BP control, and could reduce vascular damage caused by BPV [44]. Treating patients with severe BPV would therefore address drugs proven active against BPV as well as mean BP, as these would have added general cardiovascular protection.

11. Targeting BPV to Reduce Cardiovascular Risks

Increased BPV is the cause of development of arterial stiffness and left ventricular hypertrophy both of which pose a higher risk of cardiovascular events. Through BPV it may be possible to slow down or stop the structural changes in the cardiovascular system that are held accountable for heart failure, stroke, and other complications [45]. Reducing BPV can also increase vascular compliance and reduce myocardial workload thereby averting harmful effects of arterial and ventricular stiffness.

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In patients with high BPV, treatment interventions aimed at stabilizing blood pressure can reduce oxidative stress and vasculature inflammation protecting against endothelial dysfunction and inappropriately increased collagen deposition [46]. This can translate to reduced arterial stiffness and improved left ventricular compliance that are critical to long-term cardiac function. Clinical presentation of BPV also extends to individualized treatment approaches where continuous monitoring of BPV can guide therapeutic adjustment. Recent evidence also suggests that non-pharmacological interventions such as lifestyle changes to decrease stress regular physical activity and lowering dietary sodium intake can have positive impacts on BPV [47]. A combination of lifestyle and pharmacologic therapy to treat BPV can offer a more comprehensive strategy for lowering cardiovascular risk in hypertensive patients.

12. Cardiovascular Rehabilitation and its Role in Managing BPV and Cardiovascular Stiffness

Cardiovascular rehabilitation (CR) has also been promising in the management of BPV and reducing arterial and ventricular stiffness with its overall, multi-faceted system of exercise, lifestyle modification and patient education. Intermittent, moderate-intensity aerobic exercise, the focal point of CR, has been associated with reduced BPV through autonomic activity stabilization, reduced sympathetic outflow, and improved endothelial function. Greater endothelial fitness with habitual exercise is also the cause of greater arterial elasticity, and reduced sympathetic activity lowers BP peaks that are accountable for stiffness [48]. In addition, CR interventions also entail stress management, which can reduce psychological stressors accountable for triggering BP changes further stabilizing blood pressure in the long term. Lifestyle modifications, such as sodium restriction and potassium augmentation, facilitate such impacts by reducing vascular pressure and oxidative load. Through incorporation of these evidence-based interventions, cardiovascular rehabilitation, in addition to augmenting the stability of BP, also mitigates the changes at the vasculature and myocardium levels to finally improve cardiovascular health as well as counteract long-term danger in hypertensive patients [49].

13. Future Directions and Research Gap

Despite growing evidence regarding the relevance of BPV on cardiovascular risk, significant lacunae remain in understanding its specific role within arterial and ventricular stiffness. Current studies would often investigate relationships between BPV and cardiovascular outcomes but definite mechanisms by which BPV contributes to arterial wall and myocardial stiffness are not established yet. Specifically, limited information is known about the differential effects of short-term and long-term BPV on structural cardiovascular system alterations [50,51]. In addition, the majority of studies were observational; thus, causal relationships between structural alterations of the heart and vasculature and BPV are challenging to recognize. Another limitation exists in population heterogeneity within BPV research. Many of the studies are conducted among specific demographic populations, often omitting young adults or patients with first-stage hypertension. Explaining how BPV affects such groups could reveal insights into the prevention of stiffness-related cardiovascular disease at an early stage.

14. Interventions Targeting BPV to Reduce Stiffness

BPV management is essential in preventing arterial and ventricular stiffness and, as a consequence, lowering cardiovascular risk. CCBs and ACE inhibitors have proven to be beneficial in the decrease of BPV. It is still essential that more research be done to find the most effective drugs or combinations of drugs to stabilize blood pressure and lower risk associated with stiffness. One study by (Parati et al., 2024) [52] noted that long-acting CCB such as amlodipine effectively controls BPV and subsequent cardiovascular risk. Mean blood pressure level and BPV must be addressed by the authors in a bid to achieve better cardiovascular prognosis. Inflammatory responses as well as oxidative stress have disproportionate roles to play as BPV-hemmed arterial stiffness determinants. (Zhazykbayeva et al., 2020) described the molecular mechanisms by which oxidative stress and inflammation enhance cardiovascular pathologies and hypothesized that they are targets for successful interventions [53]. The findings indicate the effectiveness of combining anti-inflammatory and antioxidant therapy with antihypertensive therapy in increasing the reduction of BPV and its impact on cardiovascular stiffness.

More clinical trials would be required to attempt such multi-component interventions for effectiveness. Non-pharmacological interventions also present areas for investigation that are highly promising. Lifestyle changes, i.e., reduction of stress, exercise, diet (e.g., sodium limitation), can positively influence BPV. Research into the efficacy of these interventions on BPV in and of itself, as well as on arterial and ventricular stiffness, is essential to create wide-ranging, multi-faceted strategies for control of hypertension [47]. Lastly, advances in technology for monitoring, such as wearables and home-based blood pressure monitors, are an opportunity for the evaluation and management of BPV to become more integrated in everyday practice. Longitudinal research with such technology has the ability to provide useful information on the effectiveness of current BPV control in reducing cardiovascular stiffness and long-term consequences.

15. Conclusion

BPV has proven to be a significant actor in hypertension therapy with its role on cardiovascular performance, particularly arterial and ventricular stiffness. From the review, the mechanism through which BPV generates unwanted structural changes like arterial stiffening, endothelial dysfunction, and left ventricular hypertrophy through pressure overload, inflammation response, and sympathetic stimulation has been revealed. Augmented BPV has been associated with increased cardiovascular risk independent of mean BP, and this emphasizes the need for control of average BP as well as BP variability. Clarification of the influences of BPVs on cardiovascular stiffness presents a potential area for optimization of the treatment strategy of hypertensive patients. Regulating BPV potentially prevents or delays vascular aging and left ventricular dysfunction and thereby lessens the risk for heart failure, stroke, and myocardial infarction as complications. Regulation of both BP variability and average BP values. Elucidating the function of BPV on cardiovascular stiffness allows the potential of enhancing therapeutic regimen in hypertensive patients. By intervening with BPV, the clinician is able to retard or prevent vascular aging and left ventricular dysfunction thereby reducing the risk of complicating conditions such as heart failure, stroke, and myocardial infarction. Drug and lifestyle interventions that attenuate BPV can improve prognosis in patients with hypertension emphasizing the importance of a multi-modal treatment of such patients.

Conflicts of Interest: The authors declare no conflicts of interest.

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