

Review Article

Dysrhythmias and Hypertension

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Abstract

More than a quarter of the population of both the United States and India have a diagnosis of hypertension (HTN). HTN can lead to multiorgan dysfunction, including hypertensive heart disease. Despite the well understood morbidity and mortality associated with HTN, only 48.3% of the United States' and 10.7–20.2% of India's hypertensive population are adequately treated. Hypertensive heart disease is the result of a complex interplay of several factors, which expose the patient to an increased risk of dysrhythmias and sudden cardiac death. Management of dysrhythmias in the setting of hypertensive heart disease is similar to normotensive patients, but with a focus on optimal blood pressure, which can often reverse the pathologic cardiac remodeling and reduce the burden of dysrhythmias.

Key words: Hypertension, Blood Pressure, Dysrhythmias, Arrhythmias, India, United States, US

Background

Cardiovascular disease is the leading cause of death in the world,^[1] as well as the United States and India for the past 80+ years^[2] and 16 years,^[3] respectively. The death rate per 100,000 population in the United States is 262.3^[4] and India is 209.1.^[5] There are a variety of risk factors for cardiovascular disease, but likely none more significant than hypertension (HTN).^[6] More than a quarter of the population of both the United States (29.0%)^[7] and India (29.8%)^[8] have a diagnosis of HTN. Despite the well understood morbidity and mortality associated with HTN, only 48.3% of the United States^[7] and 10.7–20.2% of India's^[8] hypertensive population are adequately treated. Historically, HTN has been defined as a blood pressure (BP) >140/90 mmHg,^[9] but a change to >130/80 mmHg has been recommended^[10] following the SPRINT Trial.^[11] This is would result in a dramatic increase in the prevalence of HTN throughout the world, including up to 46% of the entire United States population.^[12] The patients responsible for this increase in prevalence would primarily be younger,^[13] which could be beneficial as several studies have shown that BP > 130/80 mmHg is associated with poorer outcomes in patients <65 years old.^[14–16] In addition to ischemic heart disease, stroke, vascular disease, and renal insufficiency, HTN can cause hypertensive heart disease, even with BPs of 120–139/80–89 mmHg.^[17,18]

Hypertensive Heart Disease

Hypertensive heart disease is the result of a complex interplay of several factors, particularly mechanical stress, inflammation, and the renin angiotensin aldosterone system (RAAS), and is graded in four degrees of severity with a focus on the left ventricle (LV).^[19]

1. Isolated LV diastolic dysfunction without hypertrophy
2. LV diastolic dysfunction with concentric hypertrophy
3. Clinical heart failure (HF) with preserved ejection fraction
4. Dilated cardiomyopathy with HF and reduced ejection fraction

Mechanical stress on the heart from increased afterload induces hypertrophy through parallel addition of sarcomeres.^[20,21] In addition, this stress leads to increased intramyocardial pressure^[22] and impaired cardiac perfusion. This issue is particularly present in subendocardial tissue, where the highest extravascular compressive forces occur.^[23] Similar to cardiac tissue, coronary arterioles undergo medial hypertrophy, as well as intimal hyperplasia in response to HTN.^[24] Cardiac and arterial hypertrophy exacerbate each other and result in ischemia, then eventually replacement fibrosis.^[25]

Inflammation is also known to have a role in the pathogenesis of hypertensive heart disease. While it is uncertain

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if inflammation is caused by HTN or vice versa,^[26] it is well known that hypertensive patients have elevated markers of inflammation.^[27] One explanation for the link is the frequent presence of inflammatory comorbidities (obesity, DM, etc.) in patients with HTN.^[28,29] Inflammation causes hypertensive heart disease through several mechanisms. Titin, a large protein of the sarcomere, is an important regulator of cardiac stiffness^[30] and inflammation is known to impair titin relaxation.^[31] In addition, inflammation is known to promote endothelin-1 production from endothelial cells.^[32] Endothelin-1 induces vasoconstriction, hypertrophy,^[33] and generation of superoxide,^[34] as well as endothelial to mesenchymal transition.^[35] This transition leads to coronary microvascular disease (CMD) through vessel rarefaction and fibrosis,^[36] which contributes to the ischemic process discussed earlier.

In addition, the renin–angiotensin–aldosterone system plays an important role in hypertensive heart disease, particularly in the setting of primary aldosteronism and renal artery stenosis.^[10] Activation of systemic and/or local RAAS^[37,38] induces interstitial fibrosis and endothelin-1 production.^[39]

Tachydysrhythmias

Ventricular Dysrhythmias

While hypertensive heart disease causes ventricular dysfunction, it also predisposes patients to ventricular dysrhythmias in proportion to the degree of hypertensive heart disease.^[40-43] These changes include prolongation of action potential duration due to remodeling of gap junctions^[44] and resultant dispersion of repolarization.^[45] These cellular derangements combined with tissue fibrosis and scar from CMD^[41] may lead to arrhythmogenic impulse formation and abnormal electrical conduction patterns. The most common ventricular dysrhythmia in this population is premature ventricular beats (PVBs),^[46] but patients can also experience non-sustained and sustained ventricular dysrhythmias.^[47-49] In fact, patients with HTN have 30% higher risk of sudden cardiac death (SCD), which increases proportionally with degree of HTN.^[50]

While optimal BP control has regularly been shown to reverse left ventricular hypertrophy (LVH), the impact on SCD risk is less consistent.^[51,52] The explanation for this discordance is likely related to the type of antihypertensive medication as well as the degree of myocardial substrate alteration and presence of associated comorbidities (ischemic heart disease, etc.). While all antihypertensive medications can reverse LVH to varying degrees,^[53] non-potassium-sparing diuretics, particularly thiazide diuretics, can increase the risk of SCD.^[54,55] This is thought to be due to hypokalemia,^[56] prolongation and dispersion of repolarization,^[57,43] and associated electrogenic early and delayed after depolarizations.^[58] Interestingly, potassium supplementation appears to negate this effect in loop diuretics, but not thiazide diuretics.^[54,55]

When encountering a patient with ventricular dysrhythmias, medications should be reviewed for pro-arrhythmic potential, social history assessed for alcohol and/or stimulant use, blood work obtained (complete metabolic profile and thyroid function), a 12-lead electrocardiogram to assess baseline conduction, presence of LVH, and possibly determine the site(s) of origin of PVBs, a 24 h Holter to evaluate for potential dysrhythmias and/or ventricular ectopy burden, and a transthoracic echocardiogram to evaluate cardiac structure and function.^[59] If there is concern for an infiltrative process or underlying ischemia, consider a cardiac MRI or ischemia evaluation (stress test and/or coronary angiography), respectively.^[59]

Management of patients with HTN and ventricular dysrhythmias is similar to normotensive patients, but it is important to recognize special situations that preclude the use of certain medications. In the setting of reduced systolic function (degree 4 hypertensive heart disease), calcium channel blocking agents,^[60-62] Class I agents,^[63] sotalol,^[64] and dronedarone^[65] should be avoided. In addition, as hypertensive heart disease patients can have prolongation of cardiac repolarization, care should be taken when considering Class III antiarrhythmic agents due to associated risks of Torsades de Pointes, although this risk may be less with amiodarone than other Class III agents.^[66,67] In the past, Class I and non-amiodarone Class III antiarrhythmics have been contraindicated in the setting of significant LVH^[68] due to a presumption that amiodarone had less risk of inducing dysrhythmias. However, an observational study of 537 patients with LV wall thickness >1.4 cm revealed that amiodarone actually had lower survival compared to Class I and non-amiodarone Class III agents.^[69] In addition, ablation and defibrillator implant should be considered according to the established guidelines.^[70,71] The indications for these treatment modalities are not affected by the presence or absence of HTN.^[70,71]

Atrial dysrhythmias

Although Messerli *et al.* focused on the impact of HTN on LV structure and function, HTN also impacts the atria.^[19,72] In response to increased afterload, the atria initially hypertrophy (EHRAS Class I atrial cardiomyopathy), then experience collagen deposition as LV diastolic dysfunction develops (EHRAS Class II-III).^[72] Ultimately, as a result of the hypertrophy, dilation, fibrosis, and gap junction remodeling, conduction velocity is slowed and cellular action potential duration is prolonged in a heterogeneous fashion,^[73] which leads to increased risk of atrial dysrhythmias primarily through triggering focal ectopic automaticity and disruption of uniform impulse propagation.^[44,72] In addition to an increased risk for premature atrial beats (PABs),^[75] patients with HTN are at 1.8 and 3.4 times greater risk for atrial fibrillation^[74] and supraventricular tachycardia (SVT),^[47] respectively. Similar to the ventricle, optimal BP control can reverse the pathologic remodeling^[76-78] and reduce atrial dysrhythmia burden^[44,72,79,80] to vary degrees depending on the antihypertensive class of the

agent used and the underlying degree of substrate. In general, the use of angiotensin receptor blockers as an antihypertensive appears to be associated with the most significant reduction in new-onset atrial fibrillation.^[81-83] Overall, the management of these dysrhythmias is not different between normotensive and hypertensive patients and providers should be aware of the indications and contraindications for antiarrhythmic therapy and ablation.^[68,94]

Bradydysrhythmias

Patients with hypertensive heart disease are also at increased risk for bradydysrhythmias, including high-grade AV block and sinus node dysfunction.^[84] Sinus node dysfunction and high-grade AV block in the setting of HTN are likely related to sclerosis of the sinus node artery^[85] and possibly fibrosis, leading to exit block and disruption of the AV conduction system,^[86] respectively. In addition, hypertensive patients are at increased risk for polypharmacy, which can lead to bradydysrhythmias, particularly with the combination of negative chronotropic effects of non-dihydropyridine calcium channel blockers and beta-blockers.^[87,88] Management of bradydysrhythmias is independent of HTN, primarily focuses on removing reversible factors and implant a pacemaker if none are present.^[71] It should be noted that implantation of a pacemaker is a well-accepted indication to allow for the continuation of aggressive antihypertensive medical therapy in patients with symptomatic bradycardia and difficult to control resistant HTN.

Sleep Apnea

When evaluating a patient with HTN, consider an assessment for sleep apnea as 30% of patients with HTN have sleep apnea.^[89] If unrecognized, sleep apnea can result in insufficient BP control and eventually dysrhythmias^[90] due to transient periods of hypoxia and autonomic imbalance.^[59] Up to 50% of patients with sleep apnea can experience nocturnal dysrhythmias, including sinus arrest, AV block, PVCs, NSVT, and atrial fibrillation. In addition, patients with sleep apnea are at 2.6 times greater risk of SCD.^[91] Fortunately, proper treatment with positive airway pressure therapy in patients with obstructive sleep apnea can resolve nocturnal bradydysrhythmias if function is normal during awake periods^[92] and reduce dysrhythmic events by 87%.^[93] However, positive airway pressure therapy has variable and moderate impact on HTN,^[59] so additional therapy is likely needed for optimal BP control.

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