

Hypertension: A Common but Complex Condition



Hypertension is a common condition known to cause significant cardiovascular events including death, stroke, and heart failure.^{1,2} Our understanding of the pathogenesis and optimal approaches to therapy has evolved tremendously over the past 50 years.³ Despite these advances, only 50% of individuals achieve blood pressure control according to National Health and Nutrition Examination Surveys 2015-2016 data.⁴ Hypertension remains a significant global health problem, and in this issue of *Advances in Chronic Kidney Disease*, we have put together a set of manuscripts covering several key issues in both the pathogenesis and management of hypertension.

Blood pressure measurement is perhaps the most common procedure performed in the clinical practice of medicine. Manual assessment of blood pressure is prone to several observer-based errors due to its reliance on a stethoscope and on an auscultator approach.⁵ Indeed, these “operator errors” are commonplace as a recent study of medical students attending an American Medical Association meeting illustrated that only 1 of 159 students performed all 11 elements of measuring a blood pressure correctly.⁶ Recently, there has been a movement to automated devices to measure blood pressure in clinical and clinical research settings to reduce “operator error.” Thus, the accurate measurement of blood pressure, an inherently dynamic physiologic variable which is subject to variation based on environment and situation, is paramount if we are to diagnose and manage the condition of hypertension well. Waguespack and Dwyer present a detailed discussion of blood pressure measurement considerations, including the assessment of in-office blood pressure and at-home blood pressure and ambulatory blood pressure monitoring (ABPM).

ABPM allows for multiple measurements of a patient's blood pressure throughout the course of a fixed duration of time, most commonly 24 hours. The 24-hour profile of a given patient's blood pressure provides useful information about blood pressure control and assists with the diagnosis of white coat and masked hypertension.⁷ Although ABPM has demonstrated value,⁸⁻¹⁰ it has not become widely adopted in clinical practice in many places, including the United States. Aslam and colleagues discuss the utility of ABPM, its use in patients with chronic kidney disease (CKD), kidney transplant recipients, and its limitations.

Once the diagnosis of hypertension is established, its management presents many challenges. A smaller subset of patients, estimated to be between 2% and 20%, will have so-called resistant hypertension,¹¹⁻¹³ which is defined by the American Heart Association as the requirement of 3 or more medications (with one preferably being a diuretic) to adequately control blood pressure to less than 140/90 mm Hg.¹⁴ This subset of patients will require further workup to elucidate a potentially remediable etiology. Because these conditions

involve a small number of patients, a measured approach must be taken with the diagnostic evaluation. Nagarajan and Jalal present a thorough discussion of the approach to patients with resistant hypertension, including diagnostic and therapeutic considerations.

The approach to therapy of hypertension has evolved significantly over the past 5 decades. Many seminal clinical trials have demonstrated effective treatment targets for the general population. Unfortunately, the subset of patients with CKD has not been studied as well because these patients have been systematically excluded from many studies. This has changed over the past couple of decades with the publication of several studies,¹⁵⁻¹⁸ including the recently published Systolic Blood Pressure Intervention Trial,¹⁹ targeting blood pressure control and kidney disease progression. Burgner and Lewis offer a cogent analysis of the available data to answer the question: How low do we go?

Despite numerous public health campaigns, we have been unable to control hypertension in all individuals. Recent National Health and Nutrition Examination Surveys data suggest that control is achieved in only 50% of individuals.⁴ A segment of the hypertensive population has significant disease that is resistant to therapy. One of the postulated mechanisms is an overactivity of the sympathetic nervous system. Many animal studies have shown the benefit of ablation of the renal sympathetic nerves.^{20,21} Catheter-based technologies have evolved to allow for minimally invasive approaches to ablate the renal sympathetic nerves in humans, and these procedures were seen as a potential advance in therapy for patients with hypertension. Clinical trials to date have not borne this out, but given the complexity of these patients, trial design and conduct in this area are exceedingly complex. Townsend summarizes the current data, pitfalls, lessons learned, and future approaches in conducting clinical trials in renal denervation.

Investigations into the pathogenesis of hypertension and the vascular system have led to evidence that inflammatory pathways play key roles in both the genesis of hypertension and its end-organ complications. Barrows and colleagues outline this mechanistic theory and the data that support it. Understanding this framework will be crucial in the years ahead as data continue to emerge in this area of inquiry. Molecular biology has shown that hypertension, in most cases, is a complex disorder involving multiple genetic and environmental factors. That said, the apolipoprotein L1 gene (*APOL1*) has been strongly linked to kidney disease risk and hypertension. Freedman and Robinson provide a thorough review of

the data associated with *APOL1* renal-risk variants, CKD, and hypertension.

Finally, there are a couple of special populations that require careful assessment and specific management considerations. Evaluation and management of pregnant women with hypertension is complex, and the myriad of issues surrounding the hypertensive disorders of pregnancy are reviewed by Reddy and Jim. Lastly, Samuels and colleagues address the approach to elevated blood pressure and hypertension in the pediatric population because a growing number of adolescents are afflicted with this condition.

Hypertension is a complex illness in its pathogenesis and management. Our understanding of many of these issues has advanced significantly in the last several years. It is our hope that this collection of manuscripts will provide the reader with a discussion and review of the current and emerging key issues in hypertension.

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