Beyond Office Blood Pressure Measurements: Implications of 24 Hour Blood Pressure Measurements and Measurement of Vascular Mechanics on Kidney Disease

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Over a century ago, Nikolai Korotkoff, a Russian physician reported a simple and easy way of measuring systemic arterial pressure with an inflatable cuff placed around a patient’s arm, using a stethoscope to listen to sounds in the brachial artery. Since then, this method has remained the most acceptable way of measuring arterial blood pressure in every day medical practice. Health risk estimates based on these blood pressure measurements have been validated in large population based studies. However, arterial blood pressure is a dynamic entity with an inherent variability, therefore relying on single measurements done during physician office visits may not provide an accurate estimation of health risk on an individual basis.

These observations were strengthened by data from several hypertension trials like LIFE and ASCOT, which demonstrated that even with similar blood pressure control targets some patients went on to develop cardiovascular and other end organ damage while others did not.

This has lead to the realization that other techniques to monitor blood pressure and vascular mechanics may have better clinical application in accurately measuring individual patient risk and then planning management of these patients with newer targeted goals based on these techniques.

In this talk we will discuss two such techniques:

- 24 hour ambulatory blood pressure monitor (ABPM)
- Measurement of vascular stiffness

24 hour ambulatory blood pressure monitor

Initially three factors were identified for not relying solely on office blood pressures, these were:

- Inaccuracies in methods used to measure blood pressure
- Inherent variability of blood pressure
- Tendency of blood pressure to increase in the presence of a physician (white coat effect)

Based on clinical outcome studies most hypertension guidelines recommend the use of ambulatory blood pressure monitors in the management of hypertension.

The 24 hour ambulatory blood pressure monitor is programmed to record repeated blood pressure readings for 24 hours or longer while the patient continues his activities during a usual working day. These devices are preprogrammed to measure blood pressure at intervals of 15-20 minutes during the day and 30-40 minutes at night. The blood pressure cuff is attached to a small cell phone sized central unit with a memory chip. At the completion of the study, this data is retrieved from the central unit into a software interface. The report generated contains raw data of all successful blood pressure readings, the times they were recorded and mean arterial pressures. Summary statistics for overall 24 hour, awake time and sleep time blood pressure recordings are also reported. In addition, diurnal variation in daytime versus night time readings are usually mentioned as a percentage dip in the blood pressure.
Recommended standards for normal ambulatory blood pressure is based on data from large studies in normotensive and hypertensive individuals. They are as follows:

- 130/80 mmHg or less for 24 hour blood pressure readings
- 135/85 mmHg or less for daytime
- 120/70 mmHg or less for nighttime blood pressure readings

The normal 24 hour blood pressure pattern demonstrates a decrease in blood pressure of 10-20% during the night which coincides with hours of sleep and is referred to as dipping.

The 24 hour blood pressure monitor identifies several patterns of blood pressure. These include:

- Normotension
- Hypertension
- White coat hypertension / effect
- Masked hypertension

Masked hypertension is a relatively recent clinical entity, in which patients have a normal clinic blood pressure and an elevated ambulatory blood pressure. This may lead to underestimation of cardiovascular risk events in these patients.

Nocturnal Hypertension or “reverse dipping” is one of the sub-types of masked hypertension. In these individuals although the day time blood pressures are well controlled, the nighttime blood pressure is elevated. 24 hour ambulatory monitoring is the only method by which this can be identified. In a recent study of African Americans with hypertension and kidney disease (AASK trial), almost 40% of subjects had uncontrolled hypertension secondary to nocturnal hypertension on ABPM.

Interestingly, in the AASK trial, like in other major trials including RENAAL and IDNT, despite very effective blood pressure control there was relentless progression of kidney disease. The results of these trials clearly demonstrate that even with reno-protective anti-hypertensive medications like ACEi and ARB, the progression of kidney disease could only be slowed down and not stopped.

Data in the AASK study on nocturnal hypertension gives compelling indication that, although most of these patients appeared were well controlled based on casual office blood pressure measurements during the trial, overall uncontrolled hypertension secondary to nocturnal hypertension may be the key to optimal management of kidney disease. A clinical trial by AASK investigators is currently underway to evaluate the effects of treating nocturnal hypertension in improving renal outcomes on kidney disease.

Measurement of Arterial Stiffness and Central Blood Pressure:

The first description of essential hypertension published in the late 19th century in Lancet utilized an arterial pulse tracing to measure blood pressure. This technique was replaced with the advent of sphygmomanometers, which are easy to use. Later, in the 20th century, it became evident that data provided by these pulse wave tracings may offer valuable insights on arterial stiffness, vascular mechanics and health than casual office blood pressure readings.

Several devices are now FDA approved for research and clinical use to measure abnormalities of these parameters. This is done using a pencil shape tonometer that is placed on the radial, carotid or femoral artery. In addition, some devices incorporate a blood pressure cuff or place EKG leads for a comprehensive vascular profile.

With each contraction of the left ventricle during systole, a pressure wave is generated and propagated forward in the arterial system. This is palpable as the peripheral pulse and represents not only the ventricular contraction but also the characteristics of the arterial tree. This pressure wave is then reflected back at multiple peripheral arteries that are the branch points of small muscular arteries and arterioles.
Thus the final pressure wave form that we see is the summation of the forward traveling wave generated by ventricular contraction and the backward traveling wave reflected at peripheral branch points of the vascular tree.

In healthy individuals with normal arteries, the reflected wave merges with the forward traveling wave in early diastole and augments coronary blood flow. In patients with stiff vascular arteries due to aging or vascular co-morbidities, the reflected wave returns faster and merges with the incident wave in systole. In such patients, not only does this result in an increase in left ventricular afterload but is also causes a decrease in coronary perfusion.

Important parameters measured with these devices are:

- Central Aortic Pressure
- Pulse Wave Velocity (PWV)
- Augmentation Index (AIx)

Unlike brachial blood pressure, these indices are not only dependent on cardiac output and peripheral vascular resistance but also the stiffness of conduit arteries and the timing and magnitude of pressure wave reflections.

Several cross-sectional and longitudinal studies have indicated the independent predictive value of these indices in predicting cardiovascular events. Since chronic kidney disease (CKD) patients are at several fold higher risk for cardiovascular disease and death, these indices acquire a greater significance in the risk assessment and management of these patients.

A large number of studies in CKD patients have demonstrated an increase in arterial stiffness parameters in renal patients when compared to non-renal patients. A clear relationship of this was demonstrated in a study of 180 patients with end stage renal disease which showed the AIx to be an independent determinant of cardiovascular and overall mortality. The adjusted risk ratio for each 10% increase in AIx was 1.51 for all cause mortality and 1.48 for cardiovascular mortality.

Given these background data on arterial stiffness and clinical outcomes, results from the CAFÉ study, a substudy of the ASCOT-BPLA trial assume further importance. The CAFÉ study used radial artery applanation tonometry and pulse wave analysis to calculate derived central aortic pressure and other parameters. Results from the CAFÉ study showed that despite similar brachial blood pressures, central aortic systolic blood pressure and pulse pressure were significantly lower throughout the study period in the amlodipine based treatment group as compared with atenolol-based treatment group. Further, there was a significant reduction of 16% in the composite clinical outcome for the amlodipine-based treatment group. The composite clinical outcome included all cardiovascular events and development of renal impairment. These studies provide additional compelling evidence that measuring vascular stiffness parameters should be an important component of comprehensive assessment and risk estimation for a patient. They also provide us with better targets for lowering cardiovascular and renal risk in our patients.

In summary, 24 hour ABPM and measurement of vascular stiffness are important diagnostic techniques that have an important role in clinical practice. In the Department of Nephrology and Hypertension at the Cleveland Clinic Foundation, we have been utilizing these devices for a comprehensive assessment of our patients and in guiding clinical practice and management. It is not uncommon in our practice to see patients that are referred for resistant hypertension despite being on multiple anti-hypertensive medications. 24 hour ABPM has been central in identifying white coat effect in a significant proportion of these patients. As a result, we are able to reduce their antihypertensive medications with follow up and to successfully manage their hypertension based on home blood pressure readings.
In other patients who are found to have elevated mean nighttime blood pressure on 24 hour ABPM, we try to restore the normal pattern of nocturnal fall in blood pressure by addressing risk factors such as sleep apnea, and adjustment of dosage and timing of anti-hypertensive medications. I would like to clarify here, however, that there is no data yet on whether restoring the night time fall in blood pressure reduces the risk factors. Yet another sub-group of patients may have masked hypertension/effect, for which we recommend changes in lifestyle, reducing work related stress and biofeedback interventions. Although international guidelines for blood pressure control have noted the prognostic importance of central blood pressure and other indices, data is not yet available to formulate formal recommendations on controlling these parameters. In our patients we estimate these measures and in specific patients who are at a higher risk, we may opt to add medications like calcium channel blockers to achieve optimal levels of these indices. In addition, we are actively involved in conducting studies to further evaluate the role and significance of arterial stiffness in patients with kidney disease and utilizing our understanding of this parameter to come up with novel and more definitive treatment options.