Review on Ambulatory Blood Pressure Monitoring For Prediction of Cardiovascular Disease

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ABSTRACT

Arterial hypertension is a major risk factor for cardiovascular disease. There is a strong association between blood pressure (BP) reduction and prevention of coronary artery disease (CAD). Ambulatory blood pressure monitoring (ABPM) is the most accurate tool to assess BP as a predictor of cardiovascular events, when compared to other methods, such as home and conventional BP measurements. ABPM has become an indispensable tool in the diagnosis and management of hypertension and its therapy. Therefore, the aim of this study to review the role of ambulatory blood pressure monitoring for prediction of cardiovascular disease.
Keywords: Ambulatory blood pressure monitoring; Cardiovascular Disease

Introduction

Arterial hypertension is a major risk factor for cardiovascular disease. Epidemiological studies have provided unequivocal evidence for the association between arterial hypertension and mortality from ischemic heart disease, cerebrovascular accident (CVA), and vascular diseases. Additionally, there is a strong association between blood pressure (BP) reduction and prevention of coronary artery disease (CAD) and CVA **(1).**

The number of individuals with uncontrolled hypertension (systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg) increased from 605 to 978 million, among other causes, influenced by population aging.4 The absolute increase of the hypertensive population should lead to an increase in the use of health services, which increases the need to identify and treat hypertension to prevent having to manage the costs of complications associated with the disease **(2)**.

The 24-hour ambulatory blood pressure monitoring (ABPM) is the most accurate tool to assess BP as a predictor of cardiovascular events, when compared to other methods, such as home and conventional BP measurements. However, in the primary health care (PHC) setting the availability and use of ABPM are below their indications, and general practitioners play a critical role in controlling hypertension **(3).**

Epidemiology of Hypertension

1-Primary Hypertension

Based on a cutoff of 140/90 mm Hg, 70% or more of American adults in their 60s and 70s have been diagnosed with hypertension. In addition, the Framingham Heart Study demonstrates that men and women aged 55 years and older with normal BP will have a 90% lifetime risk of developing hypertension; therefore, the reality is that all individuals are at risk to develop hypertension at some point in their lives **(4)**.

Hypertension is a major contributor to vascular injury and atherosclerotic disease and is the main risk factor for cardiovascular events, including strokes. Worldwide, hyper- tension remains the single largest preventable risk factor for death, resulting in more than 9.4 million deaths/year (13% global total deaths) primarily in low- and middle-income individuals. Observational data have shown that mortality risk doubles with increases in systolic BP from 120 to 140 mm Hg and from 140 to 160 mm Hg in all age groups. These data have led to determination of blood pressure targets that will provide a reduction in mortality risk. With the increasing availability of information, awareness of high BP, its diagnosis, and management in the US population has reached 82% **(5).**

2-Secondary Hypertension

Epidemiological data from large cohorts have identified secondary hypertension in approximately 10% among all hypertensive patients. Chronic kidney disease remains the major cause of the secondary form of hypertension (prevalence~4%), followed by aldosterone-mediated hypertension (prevalence ~4%), renal artery disease (prevalence ~1%), and hyper- or hypothyroidism (prevalence ~1%). Endocrine causes of abnormal BP have been identified in over 10 different endocrine disorders, providing targeted management and even curable treatment for hypertension in many patients **(6).**

Ambulatory Blood Pressure System

Accurate out-of-office blood pressure monitoring is essential for blood pressure evaluation and medical management. ABPM has been available for clinical use for more than 20 years with more than 60 years of available data since it was first described.[12] It is currently accepted as the best ambula- tory method to collect blood pressure readings, and its use has exponentially increased as part of the standard of care for hypertensive patients **(Figure 1) (7)**.

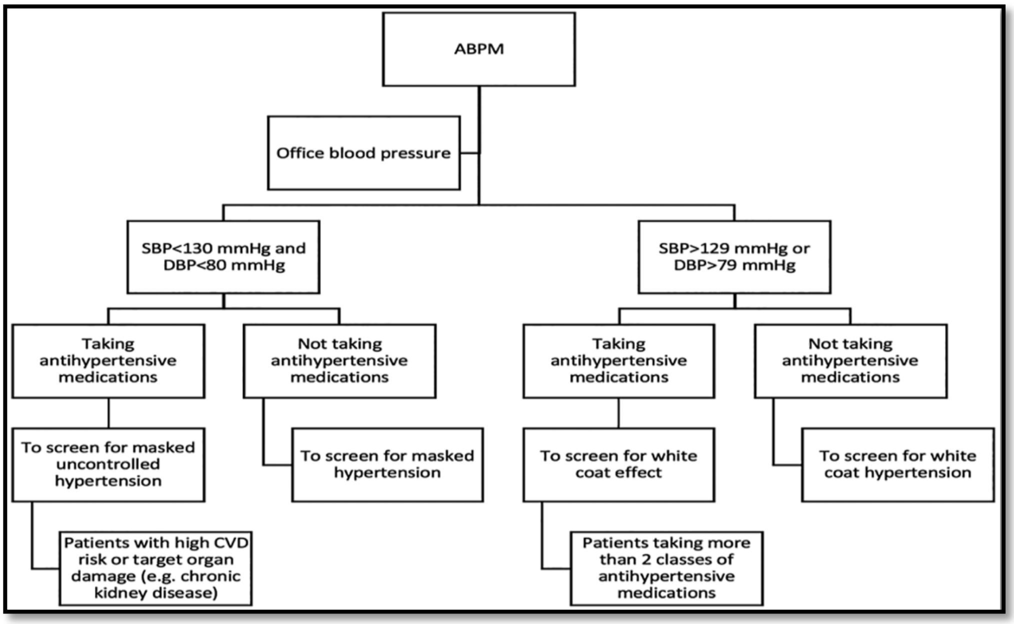

Figure (1): Recommendations for use by American College of Cardiology guidelines for the prevention, detection, evaluation, and management of high blood pressure in adults. ABPM, ambulatory blood pressure monitoring; SBP, systolic blood pressure; DBP, diastolic blood pressure. mm Hg, millimeters of mercury; CVD, cardiovascular disease.

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The market for medical devices has increased partially from the surge in demand for personalized medicine and from the need to satisfy the consumer, specifically the public, not health providers. For this reason, many devices are currently available for out-of-office blood pressure monitoring. However, the accuracy at the time of blood pressure recording has become an issue. Therefore, the Food and Drug Administration (FDA) requires that medical devices that measure blood pressure pass at least the ISO 81060- 2:2013 protocol for clinical validation, and this is based on the European Society of Hypertension International Protocol (ESH-IP) to ensure a blood pressure reading is within 5 mm Hg from a mercury device. Other common validation protocols include the Association for the Advancement of Medical Instrumentation (AAMI) and the British Hypertension Society (BHS) protocols (7).

Currently, there are several different automated blood pressure monitors that are available for out-of-office blood pressure measurements. Most of the available devices use the oscillometric technique, capable of recording 24 hours (or more) of blood pressure readings during normal daily activities and can be programmed to document readings every 10 to 30 minutes throughout the day and night. The current monitors available in the market are lightweight (weighing less than 1 kg or less than 2 pounds), measure approximately 7 × 2.5 × 9 cm, have multiple cuff sizes available, and can be used in the right or left upper extremity. Finger devices using either compression of a digital artery or waveform analysis are available for outpatient monitoring of blood pressure, but these devices have poorly validated studies supporting their accuracy and are currently not widely recommended (5).

Ambulatory blood pressure monitoring can be used in many different clinical situations and provides a more accurate physiological description of systemic blood pressure throughout an entire 24-hour time period for patients either on or off antihypertensive drugs. Ambulatory blood pres- sure monitoring is recommended for the screening and evaluation of masked hypertension, white coat hypertension, suspected episodic hypertension as pheochromocytoma , and hypotensive episodes while on medications; for the assessment of nocturnal decreases in BP; and for the follow-up of hypertensive therapies, including those in pregnant women with elevated office BP as well as individuals with orthostatic hypotension and supine hypertension (8). In clinical practice and for the primary care provider, since 2015, the United States Preventive Services Task Force has prompted individualizing blood pressure screening and management. This task force made major recom- mendations in regard to screening adults over the age of 18 years and using ABPM as a tool to confirm a suspicion or an initial diagnosis of hypertension in the clinic, which is con- sistent with the recommendations of the 2019 British guidelines for hypertension provided by the National Institute for Health and Care Excellence **(9).**

Ambulatory Blood Pressure Metrics

Systemic blood pressure selectively regulates blood flow and perfusion to each organ system based on metabolic demand, activity, time of day, and stress.

Correspondingly, it is constantly changing depending on the physiologic status of the patient. Ambulatory blood pressure monitoring ABPM provides a more physiological measurement of the "real" BP and its changes throughout the day. The correlation coefficients between office BP readings and 24-hour ABPM are 0.5 to 0.7 and 0.6 to 0.8 for systolic and diastolic blood pressure, respectively. The most commonly utilized data for clinical purposes is 24-hour average BP, daytime BP, nighttime BP, and nocturnal dipping patterns. The thresholds for normality depend on the measurement used and on the current definition of normal blood pressure. In most instances, a 24-hour mean BP of 125/75 mm Hg or less, a daytime BP of 130/80 mm Hg or less, or a nighttime BP of 110/65 mm Hg or less with a nocturnal dipping of 10% to 20% are considered normal values for ABPM **(8)**.

Circadian Blood Pressure Rhythm

Blood pressure homeostasis involves dynamic changes in the cardiovascular system based on physiological need, which also involves neurohormonal changes occurring from internal day-night clocks **(10).** Normal subjects have higher diurnal blood pressure, with a nocturnal decrease in both systolic and diastolic BP while sleeping (dipping) of 10% to 20% and a rapid increase in blood pressure in the morning related to waking up. Activity continues to be one of the main regulators of circadian blood pressure changes during the day, followed by sodium sensitivity and autonomic nervous system activity. Any disruption in circadian activity may predispose individuals to disequilibrium of the cardiovascular system, and these are the factors associated with abnormal daytime ABPM, nighttime ABPM, and nocturnal dipping in BP **(Figure 2) (11)**.

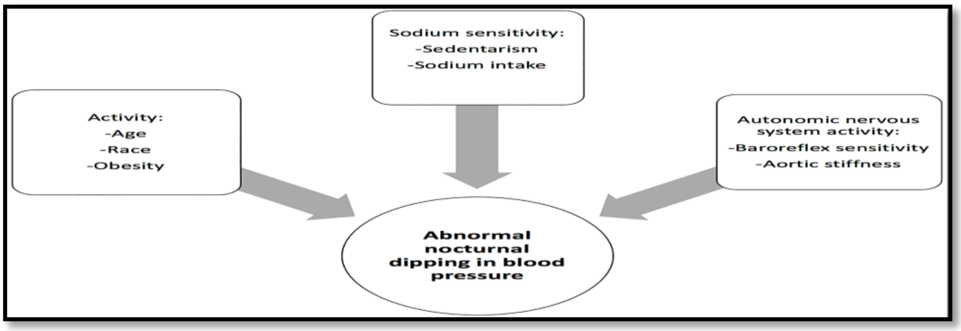

Figure (2): Major factors involved in abnormal circadian blood pressure variability.

Ambulatory BP dipping

Dipping of BP during night (nocturnal dipping) is a common normal phenomenon, occurring in more than 50% of the population, which leads to the nocturnal BP being 10% - 20% lower than a wake BP. It can be observed only in ABPM, not in HBPM or office BP. When the dip is less than 10% of daytime BP, the person is said to be a no dipper. Other alterations include reverse dipping (rise in nighttime BP) and extreme dipping (nocturnal BP falls more than 20% of the daytime BP). None dipping is different from nocturnal hypertension, which is an elevation of nighttime BP, whereas no dipping arises because of improper control and regulation mechanism of BP. No dipping and reverse dipping have been shown to be associated with more organ damage, including cardiovascular (left ventricular [LV] hypertrophy), cerebrovascular (stroke) and renal (proteinuria) disorders, with the rate being more in reverse dippers than in nondippers. Extreme dippers have been known to have increased stroke rates. Another aspect to be understood is the morning surge, which is a physiological neural and humoral response composing of activation of sympathetic system. Excess surge is known to be associated with stroke, myocardial infarction and sudden death **(12)**.

White Coat Hypertension

A diagnosis of white coat hypertension is based on an office blood pressure of 130/80 mmHg or higher in individuals with normal ABPM measurements. The prevalence of office hypertension has been estimated to be approximately 10% to 30% of patients. This condition has been described more frequently in women, and at this time, there is no evidence to suggest that it is associated with a higher cardiovascular risk than normal blood pressures. However, white coat hypertension does seem to be a risk factor for the development of sustained hypertension and possibly stroke. Although there is no evidence to support pharmacological treatment, a therapeutic focus on lifestyle modification is recommended. In addition, it is strongly recommended that these patients are followed periodically in the clinic with annual ABPM or home BP monitoring. White coat hypertension remains an evolving field, with unclear long-term outcomes, and more investigation is required. Current data are based on literature from essential hypertension studies, but ongoing studies should provide clearer guidelines for evaluation and management in clinical practice **(8).**

Resistant hypertension

Many patients of suspected resistant hypertension turn out to be white coat hypertensives, i.e., they have well controlled BP on ambulatory BP readings but falsely elevated office readings. In a study of 8295 patients with resistant hypertension, about 37.5% of patients had white coat resistance. The latest ACC/AHA guidelines recommend screening of white coat hypertension in hypertensive patients on three or more medications, with the office BP 5e10 mm Hg more than the goal, which is confirmed with normal home or ambulatory BP reading.3 Hence, ambulatory readings should be considered before dose escalation of a medication or starting a new medicine **(13)**.

Masked Hypertension

Masked hypertension occurs when a patient has out-of-office hypertension that is not apparent in clinic BP readings (ie, normal in-office blood pressure reading) but is evident with ABPM. The prevalence of masked hypertension is approximately 10% to 25% in normotensive patients and is associated with increased cardiovascular risk. Masked hypertension occurs more frequently in elderly men, smokers, patients with high alcohol intake, and patients with diabetes mellitus with or without chronic kidney disease. Poor medication adherence should be suspected in patients with masked hypertension, although there has not been a strong clinical correlation to suggest poor compliance as a major culprit **(14).** It is recommended that these patients be treated with antihypertensive drugs to achieve normotension and decrease the risk for major cardiovascular events in the future. Nocturnal blood pressure abnormalities, such as failure to decrease blood pressure during sleep (nondipping) or nocturnal high blood pressure, provide important information in studies on the association of 24-hour mean blood pressure with cardiovascular morbidity. Furthermore, patients with isolated nocturnal hypertension appear to have an increased risk of cardiovascular morbidity than to normotensive patients, although more studies are probably needed to evaluate risk and associations. In addition, the possibility of sleep apnea should be considered in these patients **(15)**.

Nocturnal hypertension

According to the latest ACC/AHA 2017 guidelines, nocturnal hypertension is defined as a BP more than 110/65 mm Hg (lowered from the earlier value of ≥ 120/70 mm Hg at night) **(8).** According to a study of more than 30,000 untreated patients and more than 60,000 patients on antihypertensive therapy (from Spanish Ambulatory Blood Pressure monitoring registry), it's prevalence was found to be more than 40% in the untreated and nearly 50% in the treated group **(16).**

Nocturnal hypertension and nocturnal dipping are separate entities; however, both of them are associated with poor cardiovascular outcomes, either separately or together. Independently, nocturnal hypertension, even when not associated with nocturnal dip, has also been shown to have association with subclinical end organ damage, especially microalbuminuria. Cerebrovascular bleeding, smoking and diabetes also correlate with nocturnal hypertension. Although female sex is more commonly associated with nocturnal dipping, the prevalence of nocturnal hypertension is found to be greater in the male population. Control of nighttime BP carries more significance in patients with once daily morning dosage of antihypertensive medication, as the BP is usually well controlled during the day. Night time BP elevation in patients on antihypertensive medication had a poor prognostic outcome in regards to cardiovascular complications (fatal and nonfatal), as the BP was controlled during the day but remained elevated at night **(17).**

Advantages and limitations

Advantages include the possibility of removal of the cuff during shower, the fact that a brachial artery transducer is not required and an error margin within 5 mm Hg of the standard mercury sphygmomanometer. Automated oscillometric BP monitors are of much use in critical care patients to detect significant changes in the pattern of BP variability **(18)**.

However, role of oscillatory method in out-of-office screening of elevated BP and hypertension can be doubtful, as the accuracy of detection of systolic and diastolic blood pressure readings is questionable. Another limitation of this technique includes the inability to accurately record BP during physical activity. The reproducibility of ABPM data is also questionable, and there often occurs inability to detect artefacts in the measurement. Patients often report discomfort while sleeping, and may choose not to get it repeated, in case required. Other limitations may include limited availability, high cost, lack of knowledge, awareness and approach of different practitioners towards ambulatory monitoring and scarcity of research over the potential benefits of ABPM **(19).**

Home BP monitoring (HBPM) and ABPM are the two modalities which can be used to monitor BP variability. HBPM refers to obtaining serial BP readings at home or at work but not in a continuous fashion, unlike ABPM. Even though there is no evidence strong enough to support the superiority of ABPM over HMPM in the management of hypertension, there are some concepts which can be used to understand it. ABPM is continuous and can elucidate the diurnal variation (especially nocturnal changes) better than HBPM, which is discontinuous monitoring at specific periods of time during the day. There is more evidence highlighting the significance of ABPM with cardiovascular events and/or mortality than HBPM **(18)**.

Validity of the readings on ABPM requires certain criteria, none of which is said to be the best. These include obtaining around 70% of the planned readings or recording of at least 14 daytime readings or obtaining at least 10 daytime and 5 nighttime readings **(20)**.

There is no doubt that the amount of clinical and epidemiological data available regarding ABPM continue to increase, but the actual scientific data comparing treatment outcomes between office BP readings and ABPM are not robust. The APTH (Ambulatory Blood Pressure and Treatment of Hypertension) trial in 1997, the THOP (Treatment of Hypertension Based on Home or Office Blood Pressure) trial in 2004, and the HOMERUS (Home versus Office measurements, Reduction of Unnecessary treatment Study) trial in 2007 failed to show any significant difference in surrogate endpoint outcomes, such as left ventricular mass changes, with a slight trend toward lower medication costs balanced by the higher costs of the ambulatory and home blood pressure equipment **(5)**.

Moreover, the idea of developing an ideal trial for absolute evidence becomes a difficult task, as noted by the Agency for Healthcare Research and Quality (AHRQ), which has estimated that a sample size of 26 000 to 57 000 patients would be needed to achieve a 10% relative risk reduction in a 10-year trial comparing office versus ambulatory blood pressure monitoring. Such a trial is unlikely to happen anytime soon **(21).**

ABPM prediction of cardiovascular disease

A prospective study demonstrated that ABPM is a better predictor of future cardiovascular events when compared to conventional BP measurements obtained in the medical office **(22).** The 24-hour ABPM is a tool capable of predicting cardiovascular outcomes in the long-term with odds ratios ranging from 1.28 to 1.4, being the only BP measurement strategy with such capacity. Therefore, based on the prognostic evidence, ABPM was selected as the reference standard for BP measurements and to assess the diagnostic accuracy of conventional BP measurements **(23).**

Compared to clinic blood pressure (BP), emerging evidence has consistently demonstrated that 24-hour ambulatory blood pressure monitoring (ABPM) provides superiority in predicting targeted organ damage and cardiovascular events in hypertensive populations (**24**). The underlying mechanisms are multifactorial. For example, ABPM offers more complete and comprehensive BP information in a longer duration. In addition, ABPM can distinguish hypertensive patterns in terms of the dipping and non-dipping BP pattern within a 24-hour circadian cycle **(25).**

The BP obtained by ambulatory blood pressure monitoring (ABPM) has shown greater accuracy of adverse events in relation to office BP, mainly in patients with masked hypertension. In individuals with normal office BP and altered ABPM, there was a higher prevalence of target organ damage (TOD), an unfavorable metabolic profile and a high risk of cardiovascular events compared to patients with normal ABPM **(26)**.

Additionally, **Mortensen et al.,(27)** revealed that Ten-year predictions obtained from ambulatory blood pressure are similar to predictions from office blood pressure. Night-time blood pressure does not improve 10-year predictions obtained from daytime measurements. For an otherwise healthy population sufficient prognostic accuracy of cardiovascular risks can be achieved with office blood pressure.

CONCLUSION

ABPM assesses the severity of BP by analyzing the pressure load on the heart and vessels so it can be used for predicting the cardiovascular risk**.**

No Conflict of interest.

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