REVIEW

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Ambulatory blood pressure monitoring: An argument for wider clinical use

ABSTRACT

Ambulatory blood pressure monitoring predicts cardiovascular risk better than office readings do. It can detect white-coat hypertension, masked hypertension, and normal and aberrant patterns of circadian variation in blood pressure. Though the clinical role of ambulatory blood pressure monitoring is currently limited, its use can be considered in many common clinical situations, eg, resistant hypertension, transplantation, pregnancy, chronic kidney disease, and dialysis. It may help in therapeutic decision-making and save money in the long term.

KEY POINTS

Current guidelines define normal daytime blood pressure as < 135/85 mm Hg, nighttime blood pressure as < 120/70, and average 24-hour blood pressure as < 130/80.

Patients without a nocturnal decline in blood pressure ("nondippers") are at higher risk of target organ damage related to hypertension.

Insurance coverage for ambulatory blood pressure monitoring is limited.

NEW USES for ambulatory blood pressure monitoring in the clinic have come to light and have the potential to significantly improve the management of hypertension, complementing office blood pressure readings. In particular, ambulatory monitoring allows for assessment of:

- Cardiovascular risk
- The "white-coat" effect, in which blood pressures are higher in the clinic than outside (currently the only indication for which Medicare and Medicaid will pay for ambulatory monitoring)
- The diurnal variation of blood pressure (which normally dips at night; "nondippers" have higher rates of target organ damage)
- Labile hypertension, with episodic hypotensive or hypertensive episodes
- Masked hypertension, in which blood pressure is normal in the office but high outside the office
- Whether blood pressure control is adequate throughout the day (TABLE 1).

Despite its potential value, ambulatory blood pressure monitoring is not widely used. Nevertheless, we believe it should be considered in a variety of clinical situations: white-coat hypertension, apparent drug resistance, hypotensive symptoms with antihypertensive medications, and episodic hypertension.

HOW IT WORKS

Patients undergoing ambulatory blood pressure monitoring wear a small device on the belt, connected by a tube to a blood pressure cuff on the arm.

To measure the blood pressure, some

TABLE 1

Our recommendations: Potential indications for ambulatory blood pressure monitoring

Suspected white-coat hypertension*

Resistant hypertension

Masked hypertension

Labile hypertension
Episodic hypertension, "spells"

Autonomic dysfunction
Orthostatic hypotension

To identify nocturnal profile of blood pressure

To assess 24-hour control of blood pressure

*Currently the only indication approved by the Centers for Medicare and Medicaid Services

TABLE 2

JNC 7 classification of blood pressure

CLASSIFICATION	PRESSURE (MM HG) SYSTOLIC*		DIASTOLIC*
Normal	< 120	and	< 80
Prehypertension	120–139	or	80–89
Stage I hypertension	140–159	or	90–99
Stage II hypertension	≥ 160	or	≥ 90

*Treatment decisions are based on the higher blood pressure category

JNC 7 = seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure

devices use the automated auscultatory method and some use the oscillometric method. Auscultatory devices have a microphone built into the cuff that detects the Korotkoff sounds, as a human observer would. A drawback of these devices is that they are subject to noise-artifact effects, and the algorithms used may not adequately compensate for certain conditions the patient may have, such as hypotension.

Most ambulatory devices now use the oscillometric technique; the term "oscillometric" refers to the oscillations in the pressure in the cuff caused by the arterial pulse pressure. Cuff placement and external noise are not significant problems, though these devices are sensitive to the patient's movements.

The device is typically set to take measurements every 15 to 20 minutes while the patient goes about his or her normal activities and every 30 to 60 minutes during sleep (timing can be adjusted).[1,2] Patients are told to keep a diary to record when they take their medication, perform any unusual physical activity, go to sleep, wake up, and do other daily activities. This information is often helpful in interpreting the results. Monitoring is usually for 24 hours.

At the end of the study, the data are downloaded into a computer. Most systems provide a graphic display of the blood pressure measurements obtained and also summary statistics for overall, day, and night blood pressures. Some typical profiles are seen in FIGURE 1.

HOW IS HIGH BLOOD PRESSURE DEFINED?

Office blood pressure

Traditionally, sporadic in-office measurements of blood pressure have been used to stratify risk and therapeutic targets, and have proven effective on a population basis. The relationship between office blood pressure and cardiovascular risk is continuous and consistent.

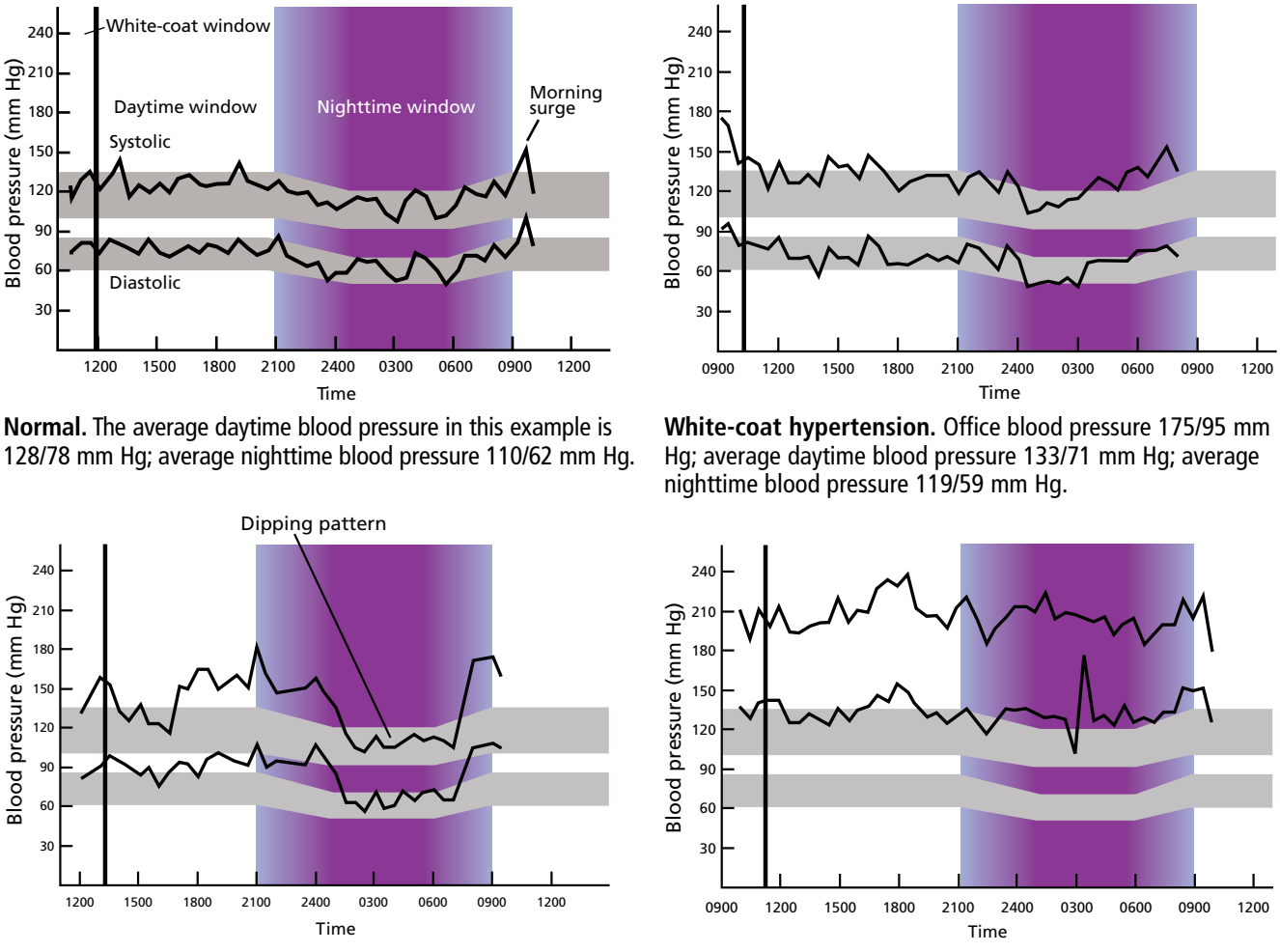
The seventh Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) classifies office-based blood pressure into four categories: normal, prehypertension, stage I hypertension, and stage II hypertension (TABLE 2). The classification is based on the average of two or more properly measured, seated blood pressure readings on each of two or more office visits.[3]

Average ambulatory pressures

How to define hypertension using ambulatory measurements is more controversial, depending on whether significance is placed on a certain level of blood pressure above the norm (the blood pressure load; see below) or on the presence of target organ damage.

For example, left ventricular hypertrophy is infrequent if the 24-hour average blood pressure is less than 135/85 mm Hg, the daytime

Patterns on ambulatory blood pressure monitoring



Normal. The average daytime blood pressure in this example is 128/78 mm Hg; average nighttime blood pressure 110/62 mm Hg.

White-coat hypertension. Office blood pressure 175/95 mm Hg; average daytime blood pressure 133/71 mm Hg; average nighttime blood pressure 119/59 mm Hg.

Hypertensive dipper. Average daytime blood pressure 147/93 mm Hg, average nighttime blood pressure 111/66 mm Hg.

Hypertensive nondipper. Average daytime blood pressure 210/134 mm Hg; average nighttime blood pressure 205/130 mm Hg.

FIGURE 1. Standardized common patterns of ambulatory blood pressure monitoring. Vertical axes show blood pressures; horizontal axes show 24-hour clock times; horizontal bands indicate normal values for 24-hour systolic and diastolic blood pressure; shaded vertical areas indicate nighttime.

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average is less than 140/90 mm Hg, or the nocturnal average is less than 125/75 mm Hg.[4,5] However, many normotensive people have lower blood pressure than noted above; one meta-analysis of more than 3,400 normotensive people found their average 24-hour blood pressure to be 118/72 mm Hg and their average daytime blood pressure 123/76 mm Hg.[6]

Based on a summary of such observational data, the American Heart Association recommends the classification of 24-hour ambulatory blood pressure data as listed in TABLE 3.[7] Similar guidelines have been proposed by the European Society of Hypertension.

Blood pressure load

The blood pressure load is the percentage of ambulatory blood pressure readings greater than 140/90 mm Hg during the day and greater than 125/75 mm Hg during sleep.

The systolic blood pressure load in normotensive people increases with age, from approximately 9% in young adults to 25% in the elderly.[8] The diastolic blood pressure load

TABLE 3

Suggested values for the upper limit of normal ambulatory pressure

	OPTIMAL	NORMAL	ABNORMAL
Daytime	< 130/80	< 135/85	> 140/90
Nighttime	< 115/65	< 120/70	> 125/75
24-Hour	< 125/75	< 130/80	> 135/85

PICKERING TG, HALL JE, APPEL LJ, ET AL. RECOMMENDATIONS FOR BLOOD PRESSURE MEASUREMENT IN HUMANS AND EXPERIMENTAL ANIMALS: PART 1: BLOOD PRESSURE MEASUREMENT IN HUMANS: A STATEMENT FOR PROFESSIONALS FROM THE SUBCOMMITTEE OF PROFESSIONAL AND PUBLIC EDUCATION OF THE AMERICAN HEART ASSOCIATION COUNCIL ON HIGH BLOOD PRESSURE RESEARCH. CIRCULATION 2005; 111:697–716.

does not seem to vary with age, averaging 3% to 4% of readings throughout all age groups.

Cardiovascular risk is increased when the daytime blood pressure load (either systolic or diastolic) is greater than 40% in people with untreated hypertension.[9]

AMBULATORY PRESSURES AND CARDIOVASCULAR RISK

It is unclear if changing a patient from a nondipper to a dipper decreases risk

Numerous prospective studies suggest that the risk of hypertensive target organ damage (including left ventricular hypertrophy) correlates more closely with ambulatory blood pressure than with office-measured blood pressure.[10–19] This difference, however, may be lessened by increasing the number of readings during one office visit.[20]

Nocturnal blood pressures may account for much of this difference; in 808 elderly hypertensive patients, the nighttime systolic blood pressure more accurately predicted cardiovascular end points than did the daytime level.[21] In a recent multivariate analysis of 1,963 hypertensive patients,[14] the risk of a cardiovascular event was independently associated with 24-hour, daytime, and nighttime ambulatory pressures, after adjustment for office blood pressure. In two separate studies of the general population, totaling more than 8,000 participants on two continents, only hypertension on ambulatory measurements (and not office blood pressures), smoking, and sex were significant predictors of cardiovascular death and death from any cause, after multivariate analysis.[17,19]

Ambulatory blood pressure monitoring also has prognostic value in patients with refractory hypertension; at similar levels of office blood pressure, cardiovascular event rates increase with ambulatory pressure.[22]

'NONDIPPERS' SEEM TO BE AT RISK

Ambulatory blood pressure monitoring is particularly useful in examining the daily and nocturnal variation in blood pressure. In people with normal blood pressure and in most hypertensive patients, the blood pressure dips by 10% to 20% during the night. "Nondippers," ie, people whose blood pressure does not dip or dips very little during sleep, seem to be at greater risk of cardiovascular events, particularly the onset of left ventricular hypertrophy,[23,24] and death.[25]

The nondipping profile of blood pressure is more common in African Americans and in patients with diabetes and chronic kidney disease, and has been associated with salt sensitivity of blood pressure.[26–28] The prevalence of diabetic nephropathy also seems to be higher in nondippers,[29] and nondipping may be associated with a faster rate of decline in glomerular filtration rate among patients with chronic kidney disease.[30,31]

Some other patients are "inverted dippers," that is, they have higher blood pressure at night. Evidence suggests that inverted dippers also have higher mortality rates.[25]

However, not all studies confirm that nondippers have a higher cardiovascular risk, perhaps because a wide range of definitions have been used.

The pathophysiologic processes underlying nocturnal hypertension are unknown. Decreased renal sodium excretory ability has been documented in some patients,[32] whereas sympathetic nervous system hyperactivity, glucocorticoid use, insulin resistance, and altered sleep patterns have been implicated in others.

Although various treatments (eg, diuretics,[33] valsartan [Diovan] taken at bedtime,[34] insulin sensitizers,[35] and renal transplantation[36]) have been suggested to restore the normal nocturnal fall in blood pressure, it remains unclear if changing a patient from being a nondipper to a dipper in and of itself decreases cardiovascular risk.

AN EARLY-MORNING SURGE IN BLOOD PRESSURE IS DANGEROUS

An abrupt rise in blood pressure upon awakening may be associated with increased risk of sudden death, myocardial infarction, and stroke in the early morning hours.[37] This reinforces the importance of maintaining blood pressure reduction throughout the 24-hour dosing period of once-daily antihypertensive agents. However, whether alteration of the antihypertensive regimen to target reduction of the morning surge in blood pressure will reduce cardiovascular risk is not clear.

WHITE-COAT HYPERTENSION

White-coat hypertension refers to elevated office measurements with normal blood pressure outside the clinic. By some estimates, the prevalence of white-coat hypertension is as high as 45% in patients with high blood pressure on an initial office reading.[38]

Ambulatory monitoring is an efficient way of diagnosing white-coat hypertension, and in fact Medicare and Medicaid will pay for ambulatory monitoring only for diagnosing white-coat hypertension. Three strict criteria need to be met for reimbursement:

- Three clinic blood pressure measurements of 140/90 mm Hg or greater;
- At least two readings lower than 140/90 mm Hg outside of the clinic; and
- No evidence of target organ injury.

Initial observational studies found no higher rate of cardiovascular disease or death in patients with white-coat hypertension.[39–41]

However, more recent studies indicate that patients with white-coat hypertension may be more similar to patients with long-standing sustained hypertension. In one study of more than 6,000 hypertensive and normotensive patients, the subset of 140 patients identified with white-coat hypertension had a higher rate of stroke over 9 years than those with normal blood pressure, more similar to that in the hypertensive group.[16] Another study found the left ventricular mass index in 119 patients with white-coat hypertension to be more similar to that in patients with stage I hypertension than that in age-matched normotensive controls.[42]

Evidence is emerging that patients with white-coat hypertension may ultimately develop sustained hypertension over time,[39] so continued follow-up is warranted in these patients. The optimal treatment, however, remains controversial.

MASKED HYPERTENSION

Masked hypertension, ie, normal office blood pressure but high ambulatory measurements, has only recently been recognized in screening clinical studies. By some estimates, as many as 10% of patients classified as normotensive by conventional office measurements have hypertension based on ambulatory monitoring.[43]

The significance of this finding is unclear, but the better correlation of ambulatory measurements with prognosis in hypertensive patients suggests that masked hypertension may be associated with increased cardiovascular risk. Whether screening large populations of patients to diagnose masked hypertension is useful and how it should best be treated need further study.

AMBULATORY MONITORING IN SPECIAL POPULATIONS

Patients with chronic kidney disease

Ambulatory blood pressure monitoring has been shown to be useful in reducing misclassification of hypertension caused by the white-coat effect and masked hypertension in patients with chronic kidney disease.[44] In this study, an average home blood pressure higher than 140/80 mm Hg (as measured by the patients themselves using a sphygmomanometer) was the best correlate of hypertension by ambulatory monitoring (defined as an average blood pressure higher than 130/80 mm Hg).

Several small, independent studies suggest that nondipping may be associated with subsequent deterioration in renal function, microalbuminuria, and death, independent of blood pressure load in this population.[31,45] Modification of the antihypertensive regimen to selectively lower nocturnal blood pressure can result in additive reduction in proteinuria. Whether reduction of nocturnal blood pressure can be a therapeutic target in patients at

By some estimates, up to 45% of patients with a high initial reading have white-coat hypertension

high risk for progression of chronic kidney disease remains to be seen.

Measuring blood pressure poses some unique challenges in patients on hemodialysis, because their intravascular volume goes down markedly after dialysis. Ambulatory blood pressure monitoring in the interdialytic period may measure the burden of hypertension better than taking the blood pressure before and after dialysis, though no evidence exists that outcomes in dialysis patients are improved with ambulatory monitoring.

Kidney transplant patients

Patients who have received renal transplants pose a particular challenge in terms of hypertension management—up to one third of them do not have optimal control. Ambulatory monitoring has been shown to help in evaluating the efficacy of antihypertensive treatment.[46]

Immediately after transplantation, many patients have nocturnal hypertension, which is underestimated and is associated with cyclosporine use. However, in the longer term, transplantation does lead to lower nocturnal blood pressure in many patients (up to 30% in some series[36]); the only predictors of response are good posttransplant renal function and normal pretransplant dipping status.[47]

In addition, ambulatory monitoring is being used to assess for hypertension in potential organ donors.

Pregnant patients

Controversy exists regarding normal values for ambulatory blood pressure in pregnancy, and some experts advocate using thresholds much lower than those used in current practice.[48] Ambulatory monitoring is more sensitive and specific than office measurements for detecting hypertension. Evidence is emerging that white-coat hypertension is common, and antihypertensive drugs may be safely withheld from this group of patients.[49] Continued monitoring throughout pregnancy is necessary, however, to detect the small number of patients with white-coat hypertension who subsequently develop preeclampsia.

COSTLY, BUT WORTH IT

An important use of ambulatory blood pressure monitoring is to assess the response of hypertension to drug treatment. When ambulatory monitoring is used to monitor therapeutic response, the regimen is changed in almost 50% of cases.[50] Recent data suggest that when ambulatory monitoring is used in managing antihypertensive therapy, fewer agents tend to be used and more patients can stop taking antihypertensive drugs altogether.[51] This may save a substantial amount of money in the treatment of newly diagnosed hypertension, as suggested by at least one cost analysis.[52]

Ambulatory blood pressure monitoring costs $150 to $300 per use. At this time, Medicaid and Medicare provide limited payment ($56–$122) for it for the diagnosis of white-coat hypertension. Home automated blood pressure measurements may be an alternative, though they cannot capture as much information as ambulatory monitoring, particularly in terms of daily and nocturnal variation.

When ambulatory monitoring is used to monitor therapeutic response, the regimen is changed in almost 50% of cases

AN ARGUMENT FOR WIDER USE

Despite the potential value of ambulatory blood pressure monitoring, it is not widely used or even available in many clinicians' offices. There are a variety of reasons: physicians do not know about it, it is expensive, and insurance does not pay for it. Despite its prognostic significance, there are no data from prospective randomized controlled trials that it is beneficial in terms of cardiovascular outcomes. For this reason, no major guideline has included ambulatory monitoring in a diagnostic algorithm of hypertension, though the Canadian Hypertension Education Program has made a general recommendation about 24-hour and home self-blood pressure monitoring to assist with diagnosing mild to moderate hypertension.[1]

Though currently limited in its clinical use, ambulatory blood pressure monitoring should be considered in a variety of clinical settings: white-coat hypertension, therapeutic decision-making (in cases of apparent drug resistance or hypotensive symptoms with antihypertensive medications), and episodic hypertension. Indeed, given its accuracy in determining risk related to blood pressure, an argument can be made for use of this technique in many patients with newly diagnosed

hypertension. Wider use of this technique could save a considerable amount of money by use of fewer agents; it may also allow for better assessment of therapeutic efficacy in patients at high risk. It is the only means of diagnosing nocturnal and masked hypertension, though optimal treatment for these conditions remains unresolved at this time. ■

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