3-1-2015

Ambulatory blood pressure monitoring: mercury rising

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Recommended Citation
Yee J. Ambulatory blood pressure monitoring: mercury rising. Adv Chronic Kidney Dis 2015; 22(2):81-85.

ACKD Advances in Chronic Kidney Disease

A Journal of the National Kidney Foundation™

Vol 22, No 2, March 2015

EDITORIAL

Ambulatory Blood Pressure Monitoring: Mercury Rising

In this issue of *Advances of Chronic Kidney Disease*, the 3 coeditors, Debbie Cohen, Jesse Goldman, and John Sim, have marshaled the efforts of 11 sets of authors to provide the readership with updates of the diagnosis and management of the most prevalent cardiovascular disease, hypertension. The 11 articles expansively cover the engaging and multidimensional relationship between hypertension and the kidney. However, this editorial will reflect on some of the vagaries encountered in the day-to-day practice of managing hypertension.

This brief vignette underscores the importance of developing and implementing blood pressure follow-up protocols with involved stakeholders and the utility of home-based blood pressure monitoring. An older man with a 30-year history of high blood pressure had, in his words, "been well controlled" by a 3-drug antihypertensive regimen until recently. However, 7 weeks after an abdominal surgery, his blood pressure, which had only been measured sporadically, was recorded as 198/105 mmHg, and he had a global headache. At 4 weeks postoperatively, his blood pressure had been recorded as normal. Notably, he had been taking only 1 antihypertensive agent then, amlodipine. Losartan and hydrochlorothiazide had been discontinued after surgery because of postoperative normotension. After restarting these, his blood pressure descended into the normal range over the next 4 weeks, while a hypertension specialist followed his case closely and communicated with the patient frequently. Over the next 5 to 6 weeks, the patient engaged in home blood pressure monitoring after the appropriate method of blood pressure measurement was taught to the patient. Three, 5-day blood pressure logs were submitted to the specialist as a surrogate of ambulatory blood pressure monitoring (ABPM). The 5-day blood pressure logs documented 4 blood pressures daily, 2 in the morning and 2 in the evening, following measurements with an oscillometric device that had been calibrated against an in-office aneroid device.[1] Over 4 weeks, the blood pressure logs revealed a decline in the patient's blood pressure to normal level but an absence of the normal decline in blood pressure during the evening and night (Table 1).

Recently, the US Preventive Services Task Force issued the following statement after conducting an exhaustive systematic review, funded by the Agency for Healthcare Research and Quality, regarding the benefits and harms of screening adults for hypertension: "On the basis of the prognostic evidence, we selected ABPM as the reference standard for BP measurement and for evaluating the diagnostic accuracy of other measurement methods.[2] We regarded daytime, night-time, or 24-hour ABPM protocols as acceptable." This statement has broad implications because noninvasive 24-hour ABPM is not routinely carried out in the United States or anywhere else for that matter, although it was conceived of nearly 50 years ago by a team led by Sokolow[3,4] and shown to correlate better than conventional mercury-based sphygmomanometry with blood pressure in the elderly patient.[5] The singular impediment in a fee-for-service environment is simply that the cost of the equipment and time to properly perform ABPM represents a nearly nil return on the investment of several thousand dollars of equipment and computers. There are defined American Medical Association Current Procedural Terminology billing codes for ABPM (93,784 and 93,788), but the only indication is for Medicare beneficiaries with an *International Classification of Diseases, Ninth Revision, Clinical Modification* code 796.2/code R03.0 that signifies an "elevated blood pressure reading without a diagnosis of hypertension," which roughly translates to "suspected 'white coat hypertension (WCH).'"[6] Strictly, WCH is defined operationally: (1) clinic/office blood pressure greater than 140/90 mmHg on at least 3 separate clinic/office visits with 2 separate measurements made at each visit, (2) at least 2 documented separate blood pressure measurements taken outside the clinic/office that are less than 140/90 mmHg, and (3) no evidence of end-organ damage. The trouble with this concept is that it omits individuals with "white coat effect," namely a hypertensive individual who manifests blood pressure elevations in-office for whichever reason.[7] Moreover, if ABPM must be repeated, the qualifying criteria must be repeated. A full 24 hours of blood pressure measurements that encompass

1548-5595/$36.00
http://dx.doi.org/10.1053/j.ackd.2015.01.001

Table 1. A 5-Day, Self-recorded Blood Pressure Log

	AM			PM		
Day	SBP (mmHg)	DBP (mmHg)	HR (bpm)	SBP (mmHg)	DBP (mmHg)	HR (bpm)
1	118	95	82	147	92	76
	135	82	82	149	89	72
2	126	82	82	152	90	71
	131	78	78	119	82	76
3	123	85	85	145	87	78
	131	81	67	134	82	72
4	134	87	84	148	87	65
	116	78	76	118	77	74
5	124	82	75	130	88	83
	122	76	73	121	79	84
Mean BP or HR	126.0	82.6	78.4	136.3	85.3	75.1
Min BP or HR	116.0	76.0	67.0	118.0	77.0	65.0
Max BP or HR	135.0	95.0	85.0	152.0	92.0	84.0
SD BP or HR	6.2	5.2	5.4	12.8	4.7	5.4

Abbreviations: DBP, diastolic blood pressure; HR, heart rate; Max, maximum; Min, minimum; SBP, systolic blood pressure; SD, standard deviation. Seated, right arm blood pressures were obtained during 2 intervals: twice from 0700 to 1000 hours (daytime) and twice from 1900 to 2200 hours (night-time). Means, minima, maxima, and SDs (measure of variability) were computed for SBP and DBP and HR during daytime and night-time intervals.

daytime and night-time blood pressures must be ascertained from the recording device to obtain any reimbursement for conduct of the study.

For non-Medicare patients, few practitioners have bothered to petition third-party payers for reimbursement of ABPM, and fewer of these payers have done so. To rub salt into the wound, the reimbursement is generally disproportionately smaller than what would be anticipated, given the effort entailed to properly read and interpret an ABPM study. The interpretation of ABPM recordings is detailed and must be correlated with the well-kept diary of the putatively hypertensive patient. ABPM interpretation is generally not taught within the curricula of Internal Medicine, Cardiology, Endocrinology, or Nephrology centers simply because there is nothing to teach from. However, ABPM is carried out routinely, and proper interpretation thereof takes place within the rubric of dedicated hypertension fellowships.

If universally applied, ABPM defines and refines the management of 4 groups of patients—Group 1: those who manifested transient hypertension; Group 2: those who incur WCH; Group 3: those who have hypertension; and Group 4: those who have "masked" hypertension (also referred to as isolated ambulatory hypertension: normal office-based blood pressure and elevated blood pressure elsewhere)—undiagnosable in the absence of ABPM. However, some cases of masked hypertension are attributable to nocturnal hypertension (nocturnal systolic blood pressure >120 mmHg).[8] The utility of ABPM in groups 1 and 2 is that individuals will not be inappropriately labeled or treated as having high blood pressure. Ironically, this would be one of the few times that medication nonadherence would be of benefit. Group 3 hypertensives who faithfully reproduce perfect blood pressure records yet truly have high blood pressure will have their hypertension exposed by ABPM. These patients mask their hypertension but do not have the masked hypertension of Group 4, defined as hypertension by ABPM or home blood pressure monitoring with normal office-based blood pressures. This phenomenon occurs in approximately 12% to 14% of those with normal office-based blood pressures and who are not treated as hypertensive patients. Masked hypertension has been correlated with left ventricular hypertrophy, increased carotid artery intima thickness, and decreased large artery distensibility. Cardiovascular disease risk may be equivalent to patients with conventional office-based hypertension. A person with a home blood pressure log that reveals masked hypertension should likely undergo a 24-hour blood pressure recording, to optimize their medical management. Lastly, masked hypertension should be sought out in patients with diabetes and/or CKD and treated accordingly.

ABPM as a monitoring tool is valuable. In the 6-month, 419 participant, treatment-blinded, Belgian Ambulatory Blood Pressure Monitoring and Treatment of Hypertension study, the hypothesis that ABPM vs conventional blood pressure measurement would result in less intensive antihypertensive therapy was fulfilled.[9] Briefly, total medication discontinuation was achieved in 26.3% of those randomized to the ABPM-monitored group vs only 7.3% ($P < .001$) in conventional, office-based group.[9] In the control group, 42.7% progressed to sustained multiple agent therapy vs just 27.2% in the ABPM-monitored group ($P < .001$). ABPM may be of particular utility in elderly patients in whom high pulse pressures correspond to impaired diastolic coronary artery filling and reduced cerebral perfusion. Overly aggressive antihypertensive therapy, which is discoverable by ABPM, can thus be identified and remediated. This risk potential has been at least partially attenuated by the global change of the hypertensive systolic pressure threshold to 150 mmHg for elderly persons by Recommendation 1 of the Eighth Joint National Committee's 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults.[10]

ABPM reporting includes facets of the blood pressure that are ignored in routine practice: circadian variation,

integrated blood pressure load, and variability of blood pressure. One of these is "dipper" status. Within the circadian rhythm of most patients, an evening-to-nocturnal "physiological" blood pressure reduction transpires.[11,12] Those who manifest this unprovoked blood pressure reduction that is normally 10% or more of the daytime systolic and diastolic blood pressures are termed, dippers. Those who do not are "nondippers" and have worse cardiovascular outcomes than their dipping counterparts, presumably from elevated nocturnal sympathetic nervous system tone. Nondippers, representing 10% to 40% of individuals who have undergone ABPM in blood pressure trials, demonstrate more left ventricular hypertrophy, brain lacunae, albuminuria, and cardiovascular mortality than dippers.[13-21]

Although, the nocturnal dipping status of systolic and diastolic blood pressures is evaluated in ABPM, the systolic pressure appears the more important of the two and overrides any effects of the 24-hour blood pressure. The hazard rate for total cardiovascular events was 1.41 (95% confidence interval, 1.03 to 1.94, $P = .03$) in the Systolic Hypertension in Europe study for each 10% increment of night-to-day systolic blood pressure.[22] In this 808-patient trial of isolated systolic hypertension with a median follow-up of 4.4 years, 12% of participants developed a major cardiovascular-related event. ABPM disclosed that increased night-time systolic pressures associated with these events; the hazard rate for cerebrovascular events increased by 0.31 and 0.20 for cardiovascular events for each 10 mmHg increment of systolic pressure. A nocturnal blood pressure of 142 mmHg was equivalent to a daytime blood pressure of 160 mmHg.

This increased burden of cardiovascular disease risk was also apparent in an ambulatory, rural Japanese population and an Italian prospective registry of cardiovascular morbidity and mortality. The Ohasama Study followed 1300 participants aged 20 years or more for 5 years.[23] Those nondippers whose 24-hour systolic pressures appeared in the highest quintile developed a significant 2.56-fold enhancement of cardiovascular mortality over the study's dippers. Equally compelling evidence has not yet been shown in blacks or patients with CKD who fail to follow a normal circadian blood pressure pattern. Lastly, nondipping may disclose a secondary source of hypertension such as sleep apnea, which our patient had, and that is characterized by enhanced sympathetic activity.[24] Kimura strongly argues that loss of dipping status is often representative of kidney disease in the absence of secondary hypertension.

A rectangle of width W and height H is certainly smaller than one of 3 W and 0.75 H, but we do not think of blood pressure in such an integrated manner. However, the concept of blood pressure load[25] is inculcated into ABPM, and only ABPM calculates this otherwise uncalculated entity when a sufficient number of blood pressures have been obtained (minima: 14 daytime and 7 nighttime blood pressures). The blood pressure load is defined by determining the number/proportion of blood pressures that exceed the hypertension threshold pressures during the daytime and night-time intervals.[26] The blood pressure load associates with left ventricular hypertrophy, especially if the systolic and diastolic blood pressure loads exceed 50% or 70%, respectively.

Greater blood pressure variability has been touted by some to predict target organ damage. The variability parameter is self-consciously reported by patients who proclaim how much their blood pressure "jumps around," notwithstanding that the patients themselves may have been jumping around during blood pressure measurements. Formally defined as the standard deviation of the systolic pressure, daytime or night-time above a group mean, blood pressure variability is not reported by all investigators. Conflicting results regarding this metric's usability and clinical utility preclude its use in an evidence-based fashion at this time.[27] For now, until further results are forthcoming, blood pressure variability's clinical utility is for want of a better word, variable.

However, the 24-hour ABPM-based pulse pressure is predictive of cardiovascular and cerebrovascular events. This metric of arterial stiffness was examined by office-based blood pressure measurement and ABPM over a mean 3.8 years of follow-up in the Progetto Ipertensione Umbria Monitoraggio Ambulatoriale study, with cardiovascular morbidity and mortality as end points.[28] Ambulatory pulse pressure clearly portended cardiovascular morbidity and mortality more than age, left ventricular hypertrophy, and nondipper status. Notably, ABPM-based pulse pressure was minimally more valuable than office-based pulse pressure, implying that the diagnosis of arterial inelasticity at a certain threshold by any blood pressure measuring technique is associated with greater cardiovascular disease.

Lastly, ABPM may lower the total cost of antihypertensive care. This is in direct alignment with the Affordable Care Act, although ABPM, which costs approximately $100 to $350 per measurement,[29] has been considered too expensive by the majority of the payers for the reasons cited earlier and cost neutral by others. For example, office visits for hypertension can be greatly reduced by ABPM, which represents an amortized piece of equipment, a clear cost savings over time for each hypertensive patient. Overall, medication costs were decreased in toto by ABPM with respect to population-based hypertension management.[9,30] In the Ambulatory Blood Pressure Monitoring and Treatment of Hypertension trial, the ABPM arm saved nearly $8 less on blood pressure medications per patient per month ($4188 vs $3390 per 100 patients per month), and physician visits were decreased. If this calculus is further verified, then arguably, most physicians would only be involved during escalation of care of hypertensive individuals, ie, prescription of second and third drugs to patients with essential hypertension.

It is time for medical personnel to stop taking blood pressures on patients when possible. This is especially relevant because a great number of blood pressures are acquired errantly for multiple reasons including the use of noncalibrated aneroid devices and failure to position patients and measuring devices appropriately for blood pressure measurements. And physicians generally should not be taking any patient's blood pressure in the majority of circumstances. Mounting evidence clearly shows that physicians, nurses, and other health care workers should

not be obtaining office-based blood pressures from patients. Aside from the patient, the blood pressure measuring device and a quiet room, devoid of television, telephones, reading materials, and other persons (ie, family members), are all that is necessary to obtain the blood pressure. Auto-repeated measurements are useful using standard oscillometrically based equipment and must become the norm at home.[31,32] It follows logically that the patient must take ownership of his blood pressure and measure it in a protocolized fashion, particularly after a significant health-related event such as our patient experienced. Until ABPM is widely deployed and to rectify the problem of inaccurate blood pressure measurement, retraining of all medical personnel is required. To this end, initiatives such as the American Medical Group Foundation's national effort to combat high blood pressure, the Measure Up/Pressure Down campaign, is laudable and achievable.[33] The Foundation has enjoined over 140 medical groups of the American Medical Group Association, representing 42 million patients, in their effort to effect successful antihypertensive therapy. Leveraging multiple stakeholders who develop high-quality best practice tools that engage providers and patients in co-ordinated care delivery systems is anticipated to successfully treat 80% of antihypertensive patients to their respective goals. In essence, high blood pressure is everyone's problem and everyone must be involved in the solution. The resolution to this problem clearly involves greater implementation of ABPM, which facilitates the diagnosis of those individuals who are truly hypertensive and permits more facile monitoring of them. Until then, continue to educate your patients on the proper method for them to participate in home blood pressure monitoring as our patient did. Home blood pressure monitoring is roughly equivalent to a 24-hour ABPM study and considered especially useful in diabetics, pregnant women, children, and individuals with CKD.[34]

The most familiar precepts are not always the truest.

—MP

Acknowledgment

The author expresses his gratitude to Raymond Townsend, MD, for his incisive contributions to this manuscript and call for action.

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Editor-in-Chief
Detroit, MI

Financial Disclosure: The author declares that he has no relevant financial interests.

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