Blood Pressure Out of the Office: Its Time Has Finally Come

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The diagnosis of hypertension includes measurement of blood pressure out of the office by either 24-hour ambulatory monitoring or home blood pressure monitoring. These methods have led to recognition of “white coat hypertension” (WCH) and “masked hypertension” (MH). Research in the 1930s first demonstrated that blood pressures in the office were often far different from those out of the office, at a time when there was no effective treatment. International attention was focused on another imminent world war and a highly controversial election in the United States. Hypertension was not a priority for concern. From the 1950s onward: (i) epidemiology linked hypertension to risk of cardiovascular disease, (ii) effective and safe drugs for treatment of hypertension appeared, (iii) randomized clinical trials demonstrated that drug treatment of hypertension is highly effective for prevention of cardiovascular disease, and (iv) advances in technology led to development of small, portable devices for recording blood pressure noninvasively at home or during usual activities. Accurate measurement of blood pressure in “real life” is now necessary and feasible for appropriate diagnosis and assessment of treatment. Out-of-office blood pressure measurement is emerging as the standard of care for hypertension.

Keywords: ambulatory blood pressure; home blood pressure; masked hypertension; white coat hypertension.

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OUT-OF-OFFICE BLOOD PRESSURE

The importance of measuring arterial pressure for diagnosis and treatment of many disorders was recognized in the 19th century. In the hospital or clinic, the stethoscope and mercury manometer became familiar symbols of medical care. The manometer is no longer present, as concerns about mercury contamination have eliminated this device; replacement by an anaeroid dial is widespread. The concept that blood pressures in an office/clinic visit may substantially differ from pressures measured out of the office is now widely recognized. Use of ambulatory blood pressure monitoring (ABPM) or home blood pressure monitoring to improve management of hypertension is now recommended by several national and international guidelines. It may seem that this concept is a recent one, dependent on the availability of modern devices that self-inflate the cuff, record pressures and even transmit to providers by telemetry. However, the history of out-of-office pressure monitoring begins more than 80 years ago; recognition of its utility was delayed by the politics and global conflict that were concurrent with the initial descriptions of this approach as well as lack of effective treatment for hypertension. A brief summary of that history is given in Table 1.

In 1930, George Brown of the Mayo Clinic in Rochester, Minnesota reported observations on the blood pressure pattern for a single patient, studied over a 3-year period. The participant was a 25-year-old man with hypertension, who requested that he be taught to take his own pressure at home 3 times a day during several changes of work, diet, and treatment with either phenobarbital (no effect) or potassium sulphocyanate. The latter was associated with a small fall in pressure.

A few years later, Ayman and Goldshine, working in Boston at the Beth Israel Hospital, reported a series of 34 individuals with hypertension. The patients or household members were instructed in use of the stethoscope, application and self-inflation of the arm cuff, detection of the Korotkoff sounds, and recording from the mercury manometer. In all 34 subjects average office pressure was higher than average home pressure, but the differences varied widely. Calculating from Ayman’s original publication, the average home systolic pressure was 16 mm Hg (95% confidence interval 13–25) lower than office pressure and the average home diastolic pressure was 11 mm Hg (95% confidence interval 8–13) lower. Approximately 60–70% of the group had lower home pressures by more than 10 mm Hg systolic pressure. The results of this new approach were published in 1940. That same year saw the election of the first 3rd term President of the United States, Franklin Roosevelt, in a highly controversial contest, and the acceleration of World War II in Europe prior to the entry by the United States in December 1941 following the Japanese bombing of Pearl Harbor. (For detailed background history, the author recommends 2 histories of this period.) It is certain that national and international politics diluted medical interest in hypertension, a disorder that, for the most part, had no discernable
Table 1. Major reports in the history of noninvasive out-of-office blood pressure

<table>
<thead>
<tr>
<th>Event/report</th>
<th>Year</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>First use of home blood pressure in trained patients</td>
<td>1940</td>
<td>Ayman et al.</td>
</tr>
<tr>
<td>Day time recording device for measurement during activities outside the office</td>
<td>1962</td>
<td>Hinman et al.</td>
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<td>Difference between ABP and clinic pressures</td>
<td>1966</td>
<td>Kain et al.</td>
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<tr>
<td>Improved correlation between out-of-office pressure and pathology</td>
<td>1966</td>
<td>Sokolow et al.</td>
</tr>
<tr>
<td>First report that antihypertensive drug treatment is effective using office pressures</td>
<td>1970</td>
<td>Veterans Administration</td>
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<tr>
<td>Day/night pressure pattern by noninvasive monitoring</td>
<td>1982</td>
<td>Pickering</td>
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<tr>
<td>Recognition of physician effect on office blood pressure</td>
<td>1983</td>
<td>Mancia</td>
</tr>
<tr>
<td>Improved prediction of cardiovascular disease by ambulatory monitoring, first report</td>
<td>1983</td>
<td>Perloff et al.</td>
</tr>
<tr>
<td>First use of “white coat hypertension”</td>
<td>1988</td>
<td>Pickering et al.</td>
</tr>
<tr>
<td>Confirming reports that ABPM confers superior prediction of cardiovascular disease.</td>
<td>1994–2006</td>
<td>Verdecchia, O’Brien, Fagard, O’Brien, Clement...</td>
</tr>
<tr>
<td>Descriptions of masked hypertension</td>
<td>2002</td>
<td>Pickering, Bobrie, Palatini</td>
</tr>
<tr>
<td>Improved prediction of cardiovascular disease by home blood pressure monitoring</td>
<td>2004–2010</td>
<td>Bobrie and others</td>
</tr>
<tr>
<td>Combination of home blood pressure monitoring with telemetry and self-titration.</td>
<td>2001–2010</td>
<td>McManus et al.</td>
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Abbreviation: ABP, ambulatory blood pressure.

cause or meaningful treatment and was, undoubtedly, not on the list of needs for military medicine. Perhaps the death of President Roosevelt in 1944 due to malignant hypertension and cerebral hemorrhage had some effect in stimulating awareness of hypertension in the medical community.35 The II World War, itself, and the post-war period dominated by the Cold War conflict and reconstruction of Europe and Japan, nonetheless fostered technical advances in electronics that could be adapted to health care. The post-war period also allowed refocus on cardiovascular disease with parallel developments in cardiovascular epidemiology, pharmacology, and eventually clinical trials.

**BLOOD PRESSURE AND CARDIOVASCULAR RISK**

Hypertension had been recognized as a predictor for future stroke and cardiac disease, especially left ventricular enlargement and heart failure since the 19th century.36 By the middle of the 20th century, prospective surveys typified by the Framingham study, using only clinic pressures, firmly established the graded relationship between level of both diastolic and systolic pressure and eventual cerebrovascular and coronary heart disease.37–39

**CARDIOVASCULAR PHARMACOLOGY**

In the 1960s, effective antihypertensive drugs became available to treat hypertension. The thiazide diuretics, spironolactone, reserpine (an adrenergic neuron depletor), guanethidine, and hydralazine could be used and were shown to be highly effective in the first randomized trials for drug treatment of severe hypertension.40 By the 1980s, beta receptor blockers and angiotensin-converting-enzyme inhibitors were developed, implemented, and shown to be effective antihypertensive drugs for prevention of cardiovascular disease. Soon, calcium channel blockers were approved and have become widely used.41 Subsequently, the angiotensin II, type 1 receptor blockers, emerged as alternatives to angiotensin-converting-enzyme inhibitors for those who could not tolerate the latter.42 Aliskiren, a direct renin inhibitor, has been approved for hypertension and is the only available member of this drug class to date.43

**CLINICAL TRIALS ESTABLISH THE VALUE OF ANTIHYPERTENSIVE DRUG THERAPY**

The effectiveness of drug treatment of hypertension in preventing cardiovascular disease, as documented in clinical trials was initially recognized by the 1970s45 and generally accepted by the mid-1980s.46 Randomized clinical trials for the treatment of hypertension used office or clinic pressures for baseline and on-treatment measurement. This required that many be treated to benefit the few, reflected in the number-needed to treat was nearly 170.47 Furthermore, those given a diagnosis of hypertension sometimes had the deleterious effect of being labeled as sick that resulted in considering themselves ill and seeking unneeded care.48 A false positive labeling of “hypertensive” had adverse consequences. Treatment of hypertension might be more efficient if accurate estimation of blood pressure outside the clinic were obtainable.

**INTRA-ARTERIAL AMBULATORY BLOOD PRESSURE MONITORING: FIRST STEPS**

In the 1960s, a small, portable device was developed for recording beat by beat arterial pressures through insertion of a brachial artery catheter.14 The length of the fluid filled catheter caused a slight overestimate of systolic pressure until
transducer tipped catheters became available. Overall, these systems were useful for studying short- and long-term variations in arterial pressure as affected by respiration, sleep, exercise, and various other activities. Intra-arterial recording was impractical and hazardous for application to study of large groups. However, the concept that measurement of arterial pressure during the entire day as a basis for evaluating hypertensive patients emerged.

NONINVASIVE AMBULATORY MONITORING

In the 1950s, the Remler Company in San Francisco, noted for its radios and electronic parts, worked with Allen T. Hinman to develop a noninvasive portable device that could sense pressure and record Korotkoff sounds on a small tape. It was small enough to be carried on a shoulder strap, like a purse or small brief case. The device required manual inflation of the cuff to occlude the brachial artery, followed by regulated deflation with sensing of the onset and cessation of the pulse. Thus, brachial artery pressure could be recorded throughout the day wherever the patient might be and during usual activity at home or work. Because manual cuff inflation by the patient was necessary, pressures could not be recorded during sleep.

Availability of the Remler device led to collaboration between its inventor, and Maurice Sokolow MD, a leading cardiologist at the University of California, San Francisco’s medical school. This group evaluated ambulatory blood pressure (day time only) in hypertension. The frequent difference between ambulatory pressure and clinic pressure was rediscovered in 1964. The better correlation between ambulatory blood pressure, compared to clinic pressure, with evidence of target organ damage (retinopathy and left ventricular hypertrophy by electrocardiogram) was established in 1966. In 1983, 43 years after Ayman and Goldshine’s publication, Dorothy Perloff, Maurice Sokoloff, and Ronald Cowan published the first report that daytime ambulatory blood pressure, in a prospective long-term follow-up study, was superior to clinic pressures for predicting future cardiovascular disease in hypertensive patients. They identified 2 patterns. Those with 10% higher clinic than ambulatory pressures had less cardiovascular disease, but those with 10% higher ambulatory pressure than clinic pressure had more compared to the other group. In that same year, Mancia et al. published observations on the behavior of blood pressure as affected by the presence or absence of a physician. A doctor’s presence briefly increased pressure, as measured by intra-arterial recording and could also be detected by the cuff method.

WHITE COAT HYPERTENSION

Improvements in devices for noninvasive blood pressure recording in the early 1980s included use of oscillometry for pulse detection, auto-inflation, improved circuitry for data storage and reduced size. Blood pressure could then be measured out of the office during the day and at night during sleep. Several devices for 24-hour ABPM became available for clinical research: Delmar Avionics, Spacelabs, Oxford, Takeda, Welch Allyn among others.

In 1988, Pickering and his colleagues published their findings that many of those with office hypertension had normal pressures when monitored during ordinary activity for the entire day and coined the term “white coat hypertension” (WCH). Since 1988, more than 1,000 publications have dealt with “WCH” (see Figure 1). Some use the terms “isolated office hypertension” or “isolated clinic hypertension” instead. Several large prospective surveys have established the importance of this diagnosis through the use of out-of-office pressure measurement. WCH is associated with significantly less cardiovascular disease than sustained hypertension in prospective studies. However, in some meta-analyses, WCH is associated with slightly higher risk for future and target organ damage compared to sustained normal blood pressure. It has not yet been established that drug treatment for WCH is effective for prevention of cardiovascular disease. Detection of WCH using ABPM is cost-effective in large part due to reduced cost of drug treatment for those with normal out-of-office pressure. There is no trial evidence to indicate that these patients are at increased risk due to lack of antihypertensive medication. Labeling a patient as hypertensive has other consequences for insurability, employment concerns, and psychological effects. The value of ABPM for eliminating anxiety due to a false positive diagnosis of hypertension, i.e., WCH, may add to its overall effectiveness.

MASKED HYPERTENSION

Since 2002 attention has been given to those with normal clinic pressures and out-of-office pressures in the hypertensive range, now called “masked hypertension” (MH). Over 400 publications dealing with this disorder have been published since its introduction (Figure 1). The prognosis for MH is nearly that of sustained hypertension and worse than either WCH or normal blood pressure. MH is more likely in younger patients, men compared to women, smokers, and those with high job strain. Those with high-normal office pressures are more likely to have MH or to progress to either MH or sustained hypertension. Those with normal office pressures without either MH at baseline or progression to sustained hypertension have less future cardiovascular disease during follow-up, compared with those who...
have MH or progress to higher pressures. During treatment of hypertension, masked-uncontrolled hypertension may be due to anxiety about taking medication. Some may take medication only a few days before the clinic visit with less adherence on days remote from the visit. Thus the clinic pressure fails to represent the overall lack of control, so-called white coat adherence. The prognosis of masked-uncontrolled hypertension may be similar to or worse than that of sustained hypertension.

In the past decade, many devices for home blood pressure measurement (HBPM) have become available. A Gallup poll reported that, by 2005, nearly two thirds of households had such devices and that nearly 50% of hypertensive patients were using them. HBPM, combined with ongoing patient feedback and surveillance is a promising strategy for detection of MH and reducing masked-uncontrolled hypertension. For effective therapy home blood pressure monitoring can be combined with self-titration of medication for those needing drug treatment to improve control of hypertension.

OUT-OF-OFFICE MEASUREMENT FOR COMPREHENSIVE MANAGEMENT OF HYPERTENSION

Hypertension is typically initially detected during clinic visits for unrelated conditions or by screening sites in various community settings (primary screening). Those considered to be hypertensive are then usually referred to clinical facilities for repeat measurement (secondary screening) and diagnostic evaluation. The potential for a false positive diagnosis of hypertension, based only on clinic pressures, with risk of unneeded treatment is a significant problem. Implementation of either ABPM or HBPM after initial screening is effective for reducing the false positive rate. Some of those who will have WCH. Others will eventually have normal pressures on repeated visits, as their pressure regresses to their average. Either ABPM or HBPM establishes an accurate baseline for comparison with on-treatment pressures if appropriate.

Once antihypertensive drug treatment is started, ongoing HBPM is becoming recognized as a highly effective basis for assessing response to treatment. Control of hypertension using HBPM is even more effective when combined with ongoing communication. When needed, change in either dose or in pattern of medications can be made without need for unnecessary clinic visits. Communication by telemetry is a basic part of this care system. Implementation of out-of-office blood pressure measurement fosters a comprehensive care system for management of hypertension and the other cardiovascular disease risk factors, particularly diabetes. At present, actual use of home blood pressure monitoring for management of hypertension in community practices, while recommended, is not well documented.

Several guidelines concur in advising that the diagnosis of hypertension for ABPM be based on average 24-hour pressures of >130/80 mm Hg (systolic/diastolic) pressures or >135/85 mm Hg for day time pressures. The normal nocturnal fall in pressures is estimated at 10–20%. For HBPM, the same thresholds, >135/85 mm Hg is advised. However, goals for on-treatment pressure are not well defined when ABPM or HBPM are used in clinical trials. Whether the same thresholds for diagnosis of hypertension will be appropriate for on-treatment pressures will depend on the relation between event rates for cardiovascular and renal disease and on-treatment ABPM or HBPM. Will lower pressures be more effective or reveal J-curve relationships as is the case of office pressures in some trials? Much more information from both clinical trials and epidemiologic surveys evaluating the impact of out-of-office pressures on response to treatment and cardiovascular outcomes is needed.

How will management of hypertension that relies on out-of-office pressure measurement be supported? 24-hour ABPM may not be feasible in all settings due to cost or availability. A detailed analysis of the economic issues is beyond the scope of this presentation. Nonetheless, some issues are readily apparent for home pressure monitoring. Will cost of devices be reimbursable? How will providers (physicians, nurse practitioners, and pharmacists) be supported for ongoing monitoring, surveillance, and adjustment of medications in the absence of office visits? The United States still relies on fee-for-service reimbursement, compared to alternate financial strategies for support of ongoing care as in the UK’s National Health Service and other national programs. Will fee-for-service reimbursement be replaced or merged with existing insurance mechanisms for cost-effective and efficient care?

ALTERNATIVES TO OUT-OF-OFFICE BLOOD PRESSURES

Ideally a cost-effective office-based method for prediction of out-of-office pressures would be an advance for reducing the time and, to some extent, inconvenience that either ABPM or HBPM demand. Smirk made this attempt by comparing "casual" blood pressures, taken in the usual setting of a busy clinic, with “basal” blood pressures taken in a quiet room, after a rest period. The difference between these 2, was named the supplemental pressure. In a large series, prognosis for cardiovascular disease was far better related to basal pressure than casual pressure and unrelated to supplemental pressures. Recording blood pressure over 6 hours on the day of a clinic visit, using an ambulatory device has been explored. This approach has been simplified by Myers et al. using the BpTru device that takes 6 blood pressures, discarding the 1st and averaging the last 5, assuming that these reduce the initial anxiety for the 1st measurement and come closer to the usual pressure for those with WCH. There is reasonable correlation between this approach and 24-hour ABPM, but the predictive power for future cardiovascular disease by using this office-based approach is unknown. Furthermore, relying on office-based pressures, alone, will fail to detect MH.

SUMMARY AND CONCLUSIONS

Measurement of arterial pressure in an office or clinic, alone, has significant limitations for optimal detection and management of hypertension. The delay in recognizing the value of out-of-office blood pressure measurement due to world events of the 1940s and 1950s has been, in some sense, compensated for by the rapid evolution of technology...
since 1950 of micro-electronics, computers, the Internet, and telemetry. Clinical trials have established the importance of treating hypertension for prevention of cardiovascular disease. Trial results may have stimulated development of more accurate and unbiased methods to measure blood pressure in "real life" compared to the artificial and highly limited use of office pressures, alone. Hypertension is a detectable and treatable global problem. Current and evolving technology for accurate and reliable measurement for blood pressure out of the office can be extended to rural and remote areas for management of hypertension and reduction of cardiovascular disease. The challenge now is to support these resources for widespread implementation and cost-effective detection and management of hypertension where ever it is a major threat to cardiovascular health.

DISCLOSURE

The author declared no conflict of interest.

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