Clinical Conference

Emerging Clinical Applications of Ambulatory Blood Pressure Recording

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Introduction:

Pilot Ambulatory Care and Education Program (PACE)

Alan S. Robbins*

This is the first Grand Rounds of the Pilot Ambulatory Care and Education program (PACE) at VAMC, Sepulveda, a UCLA teaching medical center. The purpose of PACE Grand Rounds is to provide a state of the art discussion on important topics in ambulatory medicine.

PACE is the first pilot program in the Veteran’s Health Administration that strives to improve ambulatory care to veterans and foster education and research. This patient centered system provides comprehensive, continuous, coordinated and cost-effective care through academic global-care teams which integrate inpatient and outpatient medical training for residents and students. It utilizes a multidisciplinary team model and emphasizes accessible, personalized and humanistic care provided by academic generalists and subspecialists.

This plot grew out of a major conference on Ambulatory Care and Education in 1988 sponsored by Veterans’ Health Administration Western Region and Western Medical Schools (1). One of its major recommendations was to develop pilot programs to test ambulatory care and education models and vigorously evaluate them so that cost-effective approaches could be generalized to the VA health care system. The PACE project includes many important facets: a matrix management system; conversion of an old inpatient building to an ambulatory care and educational center; incorporation of informatics into the education and care system; development of an integrated inpatient and outpatient educational experience for students and residents; emphasis on prevention, functional assessment and targeted interventions for chronic disease; development of randomized controlled protocols using three academic global team firms; inclusion of continuous quality improvement approaches; education using one way mirrors, video taping and patient actors; creation of an ambulatory surgery and imaging center; and most importantly evaluation of the project in terms of education, quality of care and costs (2).

As a prototype for ambulatory grand rounds, the most common and important ambulatory disorders were identified. Our faculty recommended the first grand round focus on hypertension and the controversy surrounding the efficiency of ambulatory blood pressure monitoring. This topic was felt to be particularly appropriate as it serves to highlight the importance of accurate diagnosis in an area where much attention has focused on a multiplicity of therapeutic interventions. For these rounds we have assembled some of the world’s authorities on ambulatory blood pressure monitoring to assure an enlightened discussion for our participants and readers. We anticipate this to be the first of many timely discussions of important topics in the ambulatory setting.

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Preamble: Ambulatory Blood Pressure Monitoring

Mohinder P. Sambhi*

Preamble

Given the marked variability of blood pressure under daily physiological conditions, it is indeed surprising that the casual measurements taken in the clinic have hitherto provided as much useful diagnostic and therapeutic information as they have in the management of patients with hypertension. Nevertheless, the measurement of clinic or office blood pressure represents a “spot check” under “contrived” circumstances and its limitations are easy to comprehend. Accordingly over the years, attempts have been made to sample blood pressure readings during the interim periods between clinic visits. The methods have included frequent-often daily-recordings of home blood pressures by the patient or a family member, the use of automated, noninvasive blood pressure monitors for limited periods, usually 12 to 24 h, and invasive intra-arterial recording during various daily activities including exercise. The use of the ambulatory devices discussed here entails complex, albeit hopefully not insurmountable, problems of technique and procedure. In addition, there is a serious lack of normal values.

This symposium does not deal with the analysis of collected data on ambulatory blood pressure recordings, but rather attempts to assess the current status of the potential clinical application of these devices as an integral part of the diagnosis, management, and treatment of hypertension. The presentations are by recognized experts in the field. Professor Perry illustrates the potential value of frequent home blood pressure recordings made at a time when there was a valid justification for obtaining several readings daily. The predictive value of these data has been contrasted with that of office pressures obtained by the Veterans Administration’s special Hypertension Screening and Treatment Program which includes the largest available data set of its kind. Professor Lund-Johansen comments on the complementary role of ambulatory blood pressure monitoring when combined with the unique long-term hemodynamic followup data collected by his group in hypertensive patients. The well known Anglo-Italian axis of pioneers on the subject is represented by Professors Sleight and Mannic who assess the advantages and the limitations of the procedures including their use in clinical trials. Professor Reid sets the new standards for future drug testing of antihypertensive agents.

Early Patient Compliance and Blood Pressure Control Using Home Readings

H. Mitchell Perry, Jr.*

It seems appropriate to begin a conference on ambulatory blood pressure monitoring with a look at home blood pressures since they represent the earliest attempt to use multiple measurements to approximate “usual pressure” under normal living conditions rather than during stressful clinic visits (3,4). The data presented here use “early” home blood pressures (i.e., those obtained one year after treatment began) to evaluate the efficacy of therapy. Although data after four and twelve years of treatment were also examined (5), they added little since the early segregation of patients into compliant and controlled categories tended to persist. Because the first antihypertensive medications were short acting, the home blood pressures used to control dosage had to be measured several times daily; thus, the early home blood pressure data considered here are more extensive and complete than could be easily collected today.

Home Blood Pressures as Predictors of Long-Term Survival

Methods: The first population considered here consisted of 223 consecutive white patients who were hospitalized during the 1950’s by the Hypertension Division at Washington University for treatment of severe hypertension and who survived for at least one year. Their average age was 46 years and half were women. Their pretreatment diastolic blood pressures (DBP) at hospital rest ranged from 115 mmHg to 150 mmHg; 83 had accelerated hypertension with hemorrhagic retinopathy but without azotemia (6).

In hospital, average DBP’s were controlled with the combination of hexamethonium and hydralazine. At discharge, patients were taught to measure their blood pressure and instructed to measure and record it before every dose of medicine (i.e., 4 or 5 times daily). Each patient was given an individualized regimen which varied the dose of hexamethonium according to the blood pressure. Usual instructions were to take the full dose of hexamethonium required in hospital for systolic blood pressures above 140 mmHg, a half dose for pressures from 125 to 140 mmHg, and no drug for pressures below 125 mmHg. Hydralazine dosage was only changed by the physician at clinic visits.

Patients were categorized as compliant if they had home blood pressure record sheets with 28 (i.e., an average of 2 measurements per day) or more recorded blood pressures during the fortnight exactly one year after treatment began. A patient was com-

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sidered noncompliant when no adequate sheet was available for that date (i.e., patient had not re- turned to clinic or had come without 28 recorded pressures). Compliant patients were further divided into uncontrolled (mean of $\geq 28$ DBP readings $\geq 100$ mmHg) or controlled (mean DBP $< 100$ mmHg) groups. Finally, vital status was determined for all 223 patients 15 years after treatment had begun, and month of death was determined for all who had died (6).

**Results:** About three-fourths of the 223 patients were compliant, and about half were controlled. The distribution of patients by compliance and control was very similar for the accelerated and nonaccelerated cohorts (Fig. 1).

For all 140 patients with nonaccelerated hypertension, median survival after treatment began was 144 months. For the 64 who were controlled, survival was 178 months; for the 37 compliant but uncontrolled patients, it was 150 months; and for the 36 noncompliant patients, it was 62 months (Fig. 1). The differences were significant, with $p < 0.001$.

For the 83 patients with accelerated hypertension, median survival was shorter (82 mos), and the subgroup pattern was different, with survival of compliant but uncontrolled patients being more like that of noncompliant patients than of controlled patients (Fig. 1).

**Conclusion:** Compliance and control only 1 year after therapy began was a good predictor of long-term survival, with compliant and controlled patients of both accelerated and nonaccelerated cohorts having median survivals nearly 3 times as long as noncompliant patients. Moreover, with accelerated hypertension, which progresses rapidly, control was essential to survival; with less rapidly progressive nonaccelerated hypertension, compliance was apparently relatively more important.

**Office Blood Pressures Are Less Predictive**

**Introduction:** With a cohort of more than 5,000 veterans, who began treatment 15 years ago (7), early clinic pressures gave qualitatively similar but quantitatively much smaller differences than early home pressures (8). Although the compliance and control criteria were basically the same as for the prior 223 patients, most of the veteran population had much less severe hypertension, treatment was less rigorous, and follow-up less intensive.

**Methods:** In 1972, as follow-up of the 223 severely hypertensive patients was being completed, the Veterans Administration initiated a Hypertension Screening and Treatment Program (HSTP). During 1974 and 1975, a total of 5,522 previously untreated hypertensive men began treatment with standard “step care” in 28 HSTP clinics. Their average age was 52 years; and 2,805 (51%) of them were black. Their pretreatment DBP's ranged from 90 to more than 140 mmHg; 19% had severe hypertension with DBP's of 115 mmHg or more. Patients with a clinic visit during 1976 were considered compliant, and those with DBP's below 100 mmHg at the last visit

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**Table 1. Early Compliance and Control in Clinic as Predictors of Survival**

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Noncompliant</td>
<td>1,191</td>
<td>4.0%</td>
<td>14.2%</td>
<td>31.2%</td>
</tr>
<tr>
<td>Compliant but uncontrolled</td>
<td>790</td>
<td>3.2%</td>
<td>11.7%</td>
<td>31.5%</td>
</tr>
<tr>
<td>Compliant and controlled</td>
<td>3,538</td>
<td>2.1%</td>
<td>9.6%</td>
<td>28.6%</td>
</tr>
<tr>
<td>Total</td>
<td>5,522</td>
<td>2.6%</td>
<td>10.9%</td>
<td>30.1%</td>
</tr>
</tbody>
</table>

Mortality as percent of the population in the groups 2, 5, 10, and 12 years after the 3 year period during which treatment was begun in the VA's Hypertension Screening and Treatment Program. Noncompliant indicates that there was no patient visit in 1976; Compliant but uncontrolled indicates that there was a visit in 1976 and the diastolic blood pressure at the last visit in 1976 was $\geq 100$ mmHg. Compliant and controlled indicates that there was a visit in 1976 and that the diastolic blood pressure at the last visit in 1976 was $< 100$ mmHg.
during 1976 were considered controlled. Length of survival was determined as a function of both compliance and control.

Results: There were 2,068 deaths from all causes among the 5,522 men during the 12 years from 1977 through 1988, for an overall mortality of 37.5%. For the first two years and the first five years of this period, noncompliant patients had 74% and 80% more deaths, respectively, than compliant patients; moreover, among compliant patients, uncontrolled patients had 52% and 48% more deaths than controlled patients.

At the intervals tested, compliant and controlled patients had the best survival; however, noncompliant patients who originally had the worst survival eventually caught up to and surpassed the compliant but uncontrolled patients (Table 1). The differences in 12 years survival between the three groups of veterans in the table were significant, with $p < 0.05$, but might well have been missed with smaller populations.

Conclusions
Compliance and control determined at clinic visits rather than by home blood pressures were again predictive of long-term survival, but the differences between groups for these generally milder patients were considerably smaller with 65% of the controlled patients versus 59% of the noncompliant patients surviving 12 years.

Comparison of Hemodynamic Testing and 24-Hour Blood Pressure Monitoring and Their Combined Use to Evaluate Antihypertensive Agents

Per Lund-Johansen*, Per Omvik, and William White

Increased blood pressure reflects disturbances in the hemodynamic factors determining blood pressure. The most important of these are total peripheral resistance and cardiac output (9-11). By hemodynamic testing, both at rest and during exercise, one can measure which of the hemodynamic changes are primarily responsible for the blood pressure elevation (12), including disturbances in exercise blood pressure and heart pump function. We have followed hemodynamic changes over a span of 20 years in untreated hypertensive patients. Similar methods have been used to test the efficacy of antihypertensive therapy and to establish whether the blood pressure is reduced through normalization of the abnormal hemodynamic parameters. In this paper, we describe the essential utility of ambulatory (intra-arterial, as well as indirect) recording of blood pressure in the assessment of hemodynamic status and the evaluation of daily and long-term treatment in patients with hypertension (13,14).

Hemodynamic Testing

Methods: In order to obtain accurate measurements of blood pressure during exercise, it is necessary to record pressure intra-arterially (15). It should be particularly stressed that the modern automatic recorders have limits during exercise (16). Although cardiac output and stroke volume may be determined reasonably accurately by the Echo-Doppler method during rest, this method is difficult to use during exercise, and the old dye-dilution technique (cardio-green or indigo-cyanine green) remains a more accurate method (17). Heart rate is usually obtained by electrocardiography. Cardiac index and total peripheral resistance index (TPRI) are calculated by conventional formulae (15).

In our laboratory the hemodynamic measurements are usually performed at rest in the supine and in the sitting position, and then during steady state exercise during 7 to 8 min of 50 W, 100 W, and 150 W ergometric bicycle exercise, with 10 min pauses between the work increments. After several months or years on a particular drug, the study can be repeated. During studies of the initial response to a drug, only one exercise load is used in the predrug situation (usually 100 W for 7 min). This allows resting hemodynamics to return to baseline values within one hour after which an acute drug effect may be measured.

It is generally agreed that the cardinal hemodynamic disturbance in established essential hypertension is an increased total peripheral resistance which is present at rest as well as during exercise (9-12). In young subjects, TPRI may appear "normal" during rest, but exercise studies have shown that it is clearly increased, and the increase is found in most vascular beds in the body (9-12). Cardiac output at rest is usually normal or slightly increased in early essential hypertension, but during exercise it is clearly subnormal. Heart rate tends to be increased, but stroke volume is subnormal during exercise. In young patients, the decrease is probably due to disturbances in the diastolic function of the heart, resulting from increased stiffness in the left ventricle, a very early phenomenon in essential hypertension (18).

Long-Term Hemodynamic Changes in Untreated Hypertension: We have followed hemodynamic changes during a period of 20 years in subjects with untreated hypertension (19). These patients had a progressive increase in TPRI and a reduction in cardiac index and in stroke index (Fig. 2). There was also a reduction in the reserve mechanism for oxygen transport since the arteriovenous oxygen difference decreased over time.

Limitations of Current 24-Hour Blood Pressure Monitors:
Today a large selection of lightweight portable blood pressure recorders are available. Our laboratory has tested several of these (Accutracker II, Spacelab, Del-Mar, Collin) against intra-arterial blood pressure at rest and during exercise. The technical problems, faulty recordings, and accuracy have been discussed in previous publications (16,20). It should be stressed that dynamic exercise (i.e. bicycle exercise) greatly disturbs readings in many of the systems even when the arm with the cuff is resting on a pillow and the arm muscles are completely relaxed. During rest, however, most of

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the recorders showed good agreement with the intra-arterial recordings in the laboratory. Proper instruction to the patient is essential to achieve meaningful readings during 24-hour use in daily life.

Hemodynamic Evaluation of Antihypertensive Drugs: We have previously studied hemodynamic effects both at rest and during exercise, of several classes of antihypertensive agents in more than 400 patients (22). The α-blockers, ACE-inhibitors, and calcium-antagonists all reduce the increased TPRI acutely as well as chronically and leave cardiac output undisturbed at rest and during exercise (23,24); the β-blockers behave differently. Although β-blockers with strong intrinsic sympathomimetic activity have little effect on cardiac output during rest, all β-blockers reduce exercise cardiac output and exercise heart rate (25,26). The reduction in cardiac output is usually well tolerated in patients without heart failure, but physical performance during long-lasting endurance exercise is reduced (27). Furthermore, the reduced cardiac output leads to reduction in peripheral blood flow and frequent complaints of cold hands and feet in cold environments.

We have recently tested a new calcium-antagonist (amlodipine) with our hemodynamic methods and 24-hour blood pressure monitoring (28). The hemodynamic method indicated that the blood pressure was reduced 17%, both at rest and during exercise, and the change was entirely due to reduction in TPRI. The 24-hour blood pressure observations indicated that blood pressure was well controlled during daytime and during sleep. Moreover, reduction in blood pressure was similar to that found by intra-arterial recordings. Thus, the drug tended to normalize the circulatory system. The 24-hour monitoring also demonstrated that the blood pressure was effectively controlled by one daily dose.

**Conclusion**

Hemodynamic testing in essential hypertension can measure disturbances in heart pump function and in regulation of vascular resistance both at rest and during exercise. The use of the modern lightweight portable blood pressure recorders can provide insight into the variations in blood pressure throughout the entire 24 h. Today these methods may be considered research tools which are useful in evaluating new types of antihypertensive agents. If 24-hour recorders become less expensive and more reliable, they may become useful in clinical practice, both for evaluating a patient’s hypertension and for monitoring the efficacy of antihypertensive therapy.

**Ambulatory Blood Pressure Monitoring: Clinical Use and Technical Problems**

**Giuseppe Mancia**

Human blood pressure recorded under daily life conditions is highly variable. In addition, office blood pressure is often markedly influenced by an alerting reaction to the measuring procedure. The pressor response accompanying the alerting reaction varies considerably from individual to individual (29). This could account for the limited correlation between office blood pressures and day-time or 24-hour blood pressures. It also justifies the interest in techniques which can measure day-time or 24-hour blood pressure (30).

Here I will focus on whether ambulatory blood pressure monitoring should replace office blood pressure for routine use in clinical practice.

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Ambulatory Blood Pressure Monitoring and Target Organ Damage

Twenty-five years ago Sokolow et al. (31) showed that the target organ damage from hypertension correlated more closely with the average blood pressure derived from 10 to 40 values measured during the day-time by a semiautomatic ambulatory device than with office blood pressure. This was confirmed by several more recent studies in which blood pressure was recorded not only during the day but during the whole 24-hour period either non-invasively or invasively (32-38). Increase in left ventricular mass index measured by echocardiography was more closely related to day-time or 24-hour blood pressure mean than to office blood pressure (30). This was true even when the population had only minimal changes in both blood pressure and left ventricular enlargement (33).

If the blood pressures obtained by 24-hour ambulatory monitoring are simply averaged, the assumption is being made that all values occurring throughout the day and night are equally important in the development of hypertension-related complications. This assumption, however, is rendered unlikely by cross-sectional data showing that: 1) the clinical manifestations of some major hypertension-related complications, i.e., myocardial infarction and sudden death, occur more commonly during the morning hours when blood pressure shows a marked rise from its low nighttime values (34); 2) left ventricular hypertrophy and alterations in cardiac function may correlate more closely with peak blood pressure values occurring during the day or exercise and “work” blood pressure than with blood pressure measured in more relaxed circumstances (35); and 3) for a given mean value obtained by 24-hour monitoring, the target organ damage is greater for patients with a greater variability in pressure values (32). This suggests that target organ damage from hypertension depends both on the average blood pressure and on the magnitude of the changes in blood pressure that take place over the 24-hour period (36). Marked blood pressure rises seem to be particularly important, but there is evidence that the lower blood pressure occurring during sleep is also relevant (37), implicating the whole range of blood pressure variations in the determination of hypertension-related cardiovascular damage.

Limitations of the Clinical Use of Ambulatory Blood Pressure Monitoring

Retrospective and cross-sectional observations have important limitations, and only prospective controlled studies showing that ambulatory blood pressure monitoring is a better predictor of target organ damage and hypertension-related complications than traditional office blood pressures can prove the superiority of the new approach. These studies have not yet been performed. Thus, the prognostic value of ambulatory blood pressure data and the greater importance of some ambulatory data over others is still unproven.

Furthermore, there is inadequate information regarding the normal values of ambulatory blood pressure. This seriously limits the potential usefulness of this technique, and impairs its value for diagnostic and therapeutic purposes, i.e., it makes it difficult to analyze the large number of values obtained with 24-hour monitoring to decide whether a small blood pressure rise is present or whether blood pressure has been normalized by treatment (30).

Finally, it should be emphasized that extensive clinical use of ambulatory blood pressure monitoring would greatly increase the cost in both money and time of the clinical management of hypertension. Widespread clinical use would also be limited by the inaccuracy of individual blood pressure readings which characterizes noninvasive ambulatory monitoring even with devices which are relatively accurate under resting conditions (30). Thus, for the time being, it seems best to largely restrict ambulatory monitoring to research and to employ it clinically only in selected cases.

Ambulatory Blood Pressure Recording in Clinical Trials

Peter Sleight*

The improved reliability of modern ambulatory blood pressure recording by noninvasive cuff methods has revolutionized the assessment of blood pressure changes in clinical trials. It is thought to largely avoid the problems of the “alerting” reaction (white coat hypertension) which plagues office blood pressures.

This “alerting” reaction increases the standard deviation of blood pressure readings so that far more patients are needed to distinguish the effects of different drug regimens (39, 40). Although the alerting reaction tends to diminish with time and with repeated measurement, this may not always be so (41).

Moreover, using intra-arterial (I.R) recordings neither clinical demeanor, nor changes in resting heart rate with stress, nor responses to mental arithmetic, enabled us to predict which individuals would have much lower pressure by ambulatory blood pressure than in the office (42).

Eliminating the Placebo Effect

The fall in clinic blood pressure in response to a placebo tablet has bedeviled clinical trials (43, 44). Using I.R recordings, we had to discard 20% of the subjects with normal blood pressure, recruited as hypertensives in a clinical trial (45). We have confirmed Gould et al.’s (46) original observation that the placebo effect on blood pressure becomes negligible when ambulatory blood pressure is measured. Gould et al. (46) used self-recorded home blood pressure measurement, which, although preferable to clinic blood pressure, suffered from some limitation of sample numbers, and more important-

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ly, from artefact due to the physical effect of self inflation of the cuff. This latter effect has been shown to raise blood pressure for up to 21 seconds and thus cause falsely high readings (47).

**Effect on Regression Dilution Bias**

It has recently become better recognized that imprecise measurement of a baseline variable, such as blood pressure can result in a serious underestimate of the relationship between the variable and future risk of morbidity or mortality. MacMahon et al. (48) have shown that plots between the “usual” diastolic blood pressure (from repeated measurements) give a much closer and steeper relationship between pressure and risk than do the “baseline” pressures, even when the latter consist of several readings. These corrected slopes are approximately 60% steeper than those obtained using baseline pressures.

Coates et al. (41) recently studied 100 subjects with mild to moderate hypertension referred to our laboratory after multiple office/clinic readings over 90 mmHg diastolic pressure. We repeated clinic and ambulatory blood pressures before and after one month of placebo treatment. There was a trend to slightly lower values in the second recording (1-2 mmHg). The initial diastolic blood pressure values were used to divide the subjects into the 5 quintiles of blood pressure chosen by MacMahon et al. (48) from the Framingham data which estimated regression to the mean by quadrennial remeasured blood pressure. We found that regression to the mean, underestimated the true slope by 69% using clinic measures, but by only 20% using ambulatory blood pressure. With the use of Ambulatory Blood Pressure, we have further shown that clinic measurements have seriously under-estimated the effect of salt intake and physical training on blood pressure (49).

**Implications for Clinical Trials of Drug Efficacy**

The power of a clinical comparison of drug effects to detect a change in blood pressure is greatly affected by precision of measurement.

We have examined the effect of taking from 1-8 samples from an ambulatory blood pressure monitoring record and have shown how increasing the numbers of samples reduces the standard deviation of blood pressure measurements. Even 8 samples were inadequate to characterize usual blood pressure compared with readings for the whole day (40, 50). Thus, sample size can be markedly reduced by ambulatory blood pressure monitoring (40). Alternatively, with the same number of subjects, ambulatory blood pressure allows reliable detection of much smaller differences in blood pressure between two treatments (51).

Based on the decrease in standard deviation with multiple measurements, our calculations (40) indicate that to detect a true treatment difference of 8 mmHg in systolic or 5 mmHg in diastolic pressure (quite usual treatment effects), would require 360 randomized patients using a single office pressure, 88 patients using ambulatory blood pressure monitoring in a parallel design, and 16 patients using ambulatory blood pressure monitoring in the above cross-over design.

**Cautionary Note**

It is of great importance to validate the methods of ambulatory blood pressure measurement (52, 53). The data quoted above are based on measurements we made with a modification of a stationary blood pressure apparatus no longer available (39, 40). The later commercial product has been less reliable (54).

O’Brien and O’Malley (55) reviewed the validation on 18 ambulatory systems. Only two, the Oxford Medilog and the Space Labs Systems satisfied the recent British Hypertension Society protocol. Moreover, no ambulatory blood pressure apparatus is able to measure truly ambulatory pressure, i.e., during exercise. We have found the Oxford Medilog recorder to be very accurate for use at rest, or immediately following heavy exercise, but less precise during treadmill exercise at speeds above 4 km/hr (56). Most users of ambulatory blood pressure machines advise the patient to stand still or sit when they feel the cuff inflate. For true exercise studies intra-arterial methods are essential (57).

**Ambulatory Blood Pressure Monitoring in Drug Evaluation**

A.D. Bainbridge and John L. Reid*

The introduction of portable, noninvasive ambulatory blood pressure (ABP) monitoring equipment has resulted in the British Hypertension Society guidelines for standards of accuracy and reproducibility (58). The potential role of these devices includes routine clinical practice (59), clinical trials (60) and the investigation of new drugs.

**Use of Ambulatory Blood Pressure Monitoring**

The design of a clinical trial to evaluate the efficacy of an antihypertensive agent must seek to explore both the magnitude and duration of effect, together with their relationship to the administered dose. Also of relevance are the potential for interaction with other agents, the possibility of an exaggerated hypotensive effect following the first dose, and any exacerbation of hypertension on withdrawal. Since the present trend is towards the development of longer acting, once daily preparations, ambulatory blood pressure monitoring is well suited to providing a reliable and comprehensive profile of antihypertensive effect.

The lack of a good correlation between the ambulatory profile and casual, office blood pressure measurement has implications with respect to both the design and the conduct of a clinical trial. Firstly, the ambulatory profile may prevent the inclusion of subjects who are not truly hypertensive. Secondly, the number of subjects required in a clinical trial for any given level of statistical power is dependent on the square of the standard deviation of the difference in the outcome measure. The standard deviation of the difference in diastolic blood pressure has been reported as 12.3 mmHg with office read-

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Elevated blood pressure is a major risk factor for common cardiovascular catastrophes, and the risk is

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**Epilogue**

**H. Mitchell Perry, Jr.**

Elevated blood pressure is a major risk factor for common cardiovascular catastrophes, and the risk is generally assumed to be proportional to the pressure. Blood pressure, however, can be very variable, and the degree of variability differs from person to person. Therefore, clinic pressures taken under stressful circumstances provide an unreliable index of a patient’s “usual pressure.” Some mechanism is needed to obtain a better approximation of usual pressure under conditions more typical of daily life. Even when many pressures are taken to better characterize a patient’s usual pressure, a decision regarding how to use the resulting mass of data is necessary.

Home blood pressures represented the first attempt to obtain “usual pressure” by obtaining multiple measurements. More recently, indirect ambulatory monitoring and direct intra-arterial monitoring have also provided multiple measurements; they ordinarily provide many values but only during a single 24-hour period. In contrast, daily home blood pressures provide monitoring for the entire period between clinic visits; however, for the usual mild or moderate hypertension usually only one measurement per day will be available. After the initial novelty wears off, home measurements are made in the presence of routine stresses of daily life. In addition to their monitoring function, home pressures involve both patient and family in the antihypertensive regimen, and thereby increase compliance; however, they depend heavily on the interest, ability, and ultimately on the compliance of the observer.

Ambulatory blood pressure monitoring and invasive intra-arterial recordings provide objective data which do not depend on long-term patient cooperation, although they obviously require some short-term cooperation. Intra-arterial monitoring seems unlikely to ever become widespread. Ambulatory monitoring is a different story; however, for it to live up to its potential, normal data are needed and their predictive value must be demonstrated. To the extent that pressures obtained by ambulatory monitoring are typical and hence representative of a patient’s exposure to hypertension, they should predict morbidity and mortality. In trained hands the technique is accurate and reproducible for the patient at rest, but not during exercise.

Since its inception, ambulatory monitoring has been greatly improved, although it still causes the patient inconvenience and often concern. There is a major lack of normal data and a major uncertainty as to how to best use the multitude of measurements which are obtained. What should the goal pressure be? What are the most useful parameters: the mean of all pressures or only of waking pressures; pressure variability or maximum pressure; how significant is “white coat hypertension” and how is it best avoided? In view of these uncertainties, ambulatory blood pressure monitoring needs further study and currently has only limited clinical value.
References


