Task Force IV: Clinical use of ambulatory blood pressure monitoring

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Objective To reach a consensus on the clinical use of ambulatory blood pressure monitoring (ABPM).

Methods A task force on the clinical use of ABPM wrote this overview in preparation for the Seventh International Consensus Conference (23–25 September 1999, Leuven, Belgium). This article was amended to account for opinions aired at the conference and to reflect the common ground reached in the discussions.

Points of consensus The Riva Rocci/Korotkoff technique, although it is prone to error, is easy and cheap to perform and remains worldwide the standard procedure for measuring blood pressure. ABPM should be performed only with properly validated devices as an accessory to conventional measurement of blood pressure. Ambulatory recording of blood pressure requires considerable investment in equipment and training and its use for screening purposes cannot be recommended. ABPM is most useful for identifying patients with white-coat hypertension (WCH), also known as isolated clinic hypertension, which is arbitrarily defined as a clinic blood pressure of more than 140 mmHg systolic or 90 mmHg diastolic in a patient with daytime ambulatory blood pressure below 135 mmHg systolic and 85 mmHg diastolic. Some experts consider a daytime blood pressure below 130 mmHg systolic and 80 mmHg diastolic optimal. Whether WCH predisposes subjects to sustained hypertension remains debated. However, outcome is better correlated to the ambulatory blood pressure than it is to the conventional blood pressure. Antihypertensive drugs lower the clinic blood pressure in patients with WCH but not the ambulatory blood pressure, and also do not improve prognosis. Nevertheless, WCH should not be left unattended. If no previous cardiovascular complications are present, treatment could be limited to follow-up and hygienic measures, which should also account for risk factors other than hypertension. ABPM is superior to conventional measurement of blood pressure not only for selecting patients for antihypertensive drug treatment but also for assessing the effects both of non-pharmacological and of pharmacological therapy. The ambulatory blood pressure should be reduced by treatment to below the thresholds applied for diagnosing sustained hypertension. ABPM makes the diagnosis and treatment of nocturnal hypertension possible and is especially indicated for patients with borderline hypertension, the elderly, pregnant women, patients with treatment-resistant hypertension and patients with symptoms suggestive of hypotension. In centres with sufficient financial resources, ABPM could become part of the routine assessment of patients with clinic hypertension. For patients with WCH, it should be repeated at annual or 6-monthly intervals. Variation of blood pressure throughout the day can be monitored only by ABPM, but several advantages of the latter technique can also be obtained by self-measurement of blood pressure, a less expensive method that is probably better suited to primary practice and use in developing countries.

Conclusions ABPM or equivalent methods for tracing the white-coat effect should become part of the routine diagnostic and therapeutic procedures applied to treated and untreated patients with elevated clinic blood pressures. Results of long-term outcome trials should better establish the advantage of further integrating ABPM as an accessory to conventional sphygmomanometry into the routine care of hypertensive patients and should provide more definite information on the long-term cost-effectiveness. Because such trials are not likely to be funded by the pharmaceutical industry, governments and health insurance companies should take responsibility in this regard. *Blood Press Monit* 4:319–331 © 1999 Lippincott Williams & Wilkins.

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Introduction

Ambulatory blood pressure monitoring is increasingly being used in clinical practice. During the past two decades various proposals for the diagnostic interpretation of ambulatory blood pressure recordings have been published

[1–5]. Meanwhile, prognostic data accrued, with which attempts to validate these thresholds not only in terms of intermediary cardiovascular end points [6–13], but also in terms of mortality and morbidity [7,10,12–17] were made.

Several expert committees have already issued national or international guidelines for the clinical application of ambulatory blood pressure monitoring [4,5,18,19]. During the past 10 years, international (consensus) conferences on ambulatory blood pressure measurement have been organized in Berlin (1990 [20]), Dublin (1991 [21]), New Orleans (1992), Leuven (1994 [22]), Paris (1996) and Monza (1998). For the Seventh International Consensus Conference (23–25 September 1999, Leuven, Belgium), six working groups were constituted. Before the conference each of these task forces had to prepare an overview of a specific topic. After the meeting, these review articles were amended to account for opinions aired at the conference and to reflect the common ground reached in the discussions. This article was prepared by the task force on the clinical use of ambulatory blood pressure monitoring.

Advantages of ambulatory blood pressure measurement

Pitfalls of conventional sphygmomanometry

In clinical practice blood pressure is commonly measured by conventional sphygmomanometry and auscultation of the Korotkoff sounds [23]. However, this procedure is fraught with potential errors, which may arise in the subject, the observer, the sphygmomanometer, and the overall application of the technique [24,25]. Terminal digit preference refers to the phenomenon whereby the observer rounds off the blood pressure reading to an arbitrary digit, often to a zero or a five [26,27]. Observer bias is the practice whereby the observer simply adjusts the blood pressure reading to meet a preconceived idea of what the blood pressure should be [26,28]. Observer prejudice is most likely to occur when an arbitrary dividing line is applied to diagnose hypertension or to adjust treatment [28]. Moreover, the presence of an observer, such as a nurse or a doctor, can arouse the patient and increase the patient's blood pressure [29–33]. This so-called white-coat effect can lead to overestimation of the blood pressure and hence to an incorrect diagnosis of (sustained) hypertension. The seemingly elevated blood pressure in patients with white-coat hypertension is not maintained in the absence of the observer [29–33]. Another major drawback of conventional sphygmomanometry stems from the fact that blood pressure is highly variable [34] and characterized by large diurnal fluctuations [35,36]. Single or multiple readings taken by an auscultating observer once or even several times during the day reflect a subject's true blood pressure only to a minor extent. Aneroid and electronic monitors are also used in clinical practice, although they have varying reliability and require regular calibration.

Theoretical advantages of ambulatory blood pressure monitoring

Ambulatory monitoring makes it possible to record the blood pressure in patients engaged in their normal activities throughout the whole day and to provide within 24 h a reliable estimate of their usual blood pressure [20]. In order to collect the same information, conventional measurements must be repeated at intervals of a few weeks [4,5,37]. Furthermore, the ambulatory blood pressure level is characterized by high reproducibility [38], is not subject to digit preference and observer bias [28] and is not subject to the transient rise of a patient's blood pressure in response to the clinic surroundings or the presence of the observer [32], the so-called white-coat effect [30,39,40].

Clinical trials

In view of these theoretical advantages, the investigators in the Ambulatory Blood Pressure Monitoring and Treatment of Hypertension (APTH) trial [41,42] tested the hypotheses that the use of ambulatory blood pressure monitoring in the management of hypertensive patients would lead to less intensive treatment with drugs and hence fewer side effects and that, in spite of the reduction in intensity of treatment, control of blood pressure over the whole day and protection against left ventricular hypertrophy would remain preserved.

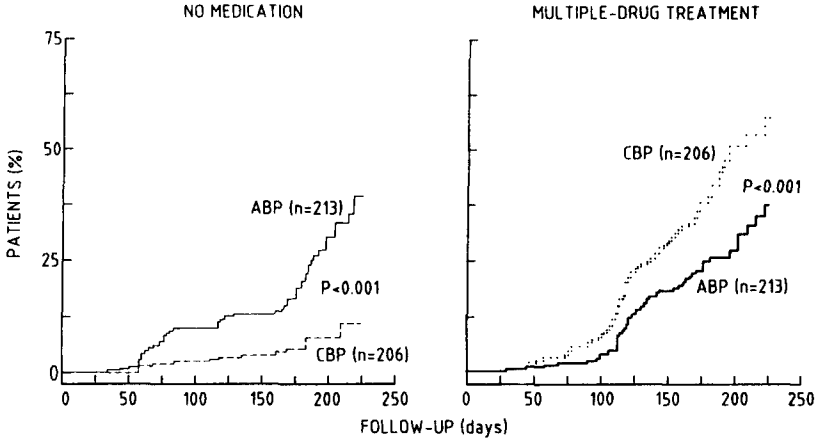
Patients were randomly allocated to be treated according to the average daytime (1000–2000 h) ambulatory blood pressure (ABP group) or the average of three sitting readings obtained by conventional sphygmomanometry (CBP group). After randomization, all patients were administered 10 mg/day lisinopril (step I). Follow-up visits were scheduled for 1 month (visit one), 2 months (visit two), 4 months (visit three) and 6 months (visit four) after randomization. The same standardized treatment regimen was applied to both groups with the goal of reaching the same target range of diastolic blood pressure, namely 80–89 mmHg [41]. The possible alterations in treatment after each of these four visits involved increasing the dose of lisinopril to its standard dose of 20 mg/day (step II), the addition of 12.5 mg hydrochlorothiazide in the morning (step III) and the addition of 5 mg/day amlodipine (step IV). For patients with known contra-indications to use of converting enzyme inhibitors, lisinopril could be substituted by 50 mg/day (step I) or 100 mg/day (step II) atenolol. If the diastolic blood pressure guiding treatment was above target (> 89 mmHg), medical treatment was intensified by one step. If the diastolic blood pressure was within the target range (80–89 mmHg), medical treatment was left unchanged. If the diastolic blood pressure guiding treatment was below target (< 80 mmHg), medical treatment was reduced by one step. The level of the target blood pressure and the treatment steps were the same for both treatment groups. This made it possible for one physician at the coordinating office to take all decisions regarding treatment in a blinded fashion [41].

After randomization, more ABP than CBP patients stopped being administered antihypertensive drug treatment (Fig. 1), because their diastolic blood pressures were less than 80 mmHg and thereafter remained below or within the target range (26.3 versus 7.3%; 4.7 versus 1.3 patients per 100 followed up for 1 month; $P < 0.001$). The opposite trend (Fig. 1) was observed for patients proceeding to sustained multiple drug treatment (27.2 versus 42.7%; 4.8 versus 8.3 patients per 100 followed up for 1 month; $P < 0.001$). Blood pressures of patients in both groups decreased ($P < 0.001$) after randomization. During the first follow-up visit, the decreases for the two treatment groups were the same, averaging 16.5/10.2 mmHg for the conventional blood pressure and 11.2/7.5 mmHg for the daytime blood pressure. Thereafter, the reduction in blood pressure in the CBP patients tended to be slightly greater than that in members of the ABP group. The final conventional and 24 h ambulatory blood pressures averaged 144/90 and 129/80 mmHg for patients in the ABP group and 140/90 and 128/79 mmHg for CBP-group patients (P values for the between-group differences ranged from 0.16 to 0.02). At the end of follow-up, electrocardiographic and echocardiographic left ventricular masses and symptoms reported for the two groups were similar. Thus, results of the APTH trial demonstrated that adjustment of antihypertensive treatment based on ambulatory monitoring, instead of on conventional sphygmomanometry, can lead to less intensive treatment with drugs with preservation of control of blood pressure, general well-being and inhibition of enlargement of left ventricles [42].

Results of two clinical trials [9,11] demonstrated that regression of left ventricular mass in patients administered antihypertensive drug treatment was more closely correlated to the decrease in the 24 h blood pressure than it was to the reduction in the clinic blood pressure, regardless of whether the latter was measured by conventional sphygmomanometry [9,11], a random-zero device [9] or a stationary automated technique (Dinamap 845; Applied Medical Research Corporation, Tampa, Florida, USA) [11]. In the Study on Ambulatory Monitoring of Blood Pressure and Lisinopril Evaluation (SAMPLE) [9], left ventricular mass index at baseline was not correlated to clinic blood pressure, but did exhibit correlations to systolic and diastolic 24 h blood pressures ($r = 0.34$ and 0.27, respectively, $P < 0.01$). The regression of left ventricular mass index was not correlated to the reduction in clinic blood pressure, but it was correlated to the reductions in the 24 h systolic and diastolic blood pressures ($r = 0.42$ and 0.38, respectively, $P < 0.01$). Treatment-induced changes in daytime and night-time blood pressures were correlated to changes in left ventricular mass index as strongly as they were to the changes in 24 h blood pressure [9].

In the Lisinopril–Isradipine (LISIS) trial [11] left ventricular mass, adjusted for sex and body size, was significantly associated with systolic and diastolic clinic blood pressures, both before ($r = 0.57$ and 0.48, $P < 0.001$ for both) and during ($r = 0.43$, $P < 0.001$ and $r = 0.27$, $P < 0.05$) antihypertensive therapy. Changes in left ventricular mass were significantly correlated to changes in blood pressure. The correlation coefficients amounted to 0.39 ($P < 0.01$) and 0.40 ($P < 0.01$) for the conventional and automated measurements of clinic systolic blood pressures, respectively, and to 0.45 ($P < 0.001$) for the average 24 h systolic blood pressure. For the corresponding diastolic measurements, these correlation coefficients were 0.27 (NS), 0.20 (NS) and 0.43 ($P < 0.01$), respectively [11]. The average 24 h blood pressure added 7.4% ($P < 0.05$) and 6.2% ($P = 0.06$) to the variance of the changes in left ventricular

Fig. 1



Kaplan–Meier estimates modelling the probability that patients would permanently stop being administered antihypertensive drug treatment during follow-up or would proceed to sustained multiple drug treatment. The differences between the patients randomly allocated to conventional (CBP, dotted and broken lines) and ambulatory (ABP, full line) measurement of blood pressure were significant ($P < 0.001$). Reproduced with permission from [42].

mass already explained in terms of the conventional and the automated measurements of clinic systolic blood pressures, respectively, and 11.2% ($P < 0.05$) and 14.5% ($P < 0.01$) for the diastolic blood pressures. In addition, the changes in daytime and night-time blood pressures also significantly ($P < 0.01$) predicted the regression of left ventricular mass [11].

General recommendations for the use of ambulatory monitoring

Guidelines [4,5,19,43] are unanimous in stipulating that only properly validated devices should be used. Such validation procedures have been standardized carefully [44–47]. Furthermore, when devices are to be used with special populations of patients, such as old subjects and pregnant women [48–50], or under special conditions, such as during exercise [51,52], a specific demonstration of accuracy for these defined subgroups and conditions is necessary [45,48]. Just as important as the equipment is the proper training of the technicians and doctors who fit the monitors or are involved in decoding or interpreting the recordings.

Theoretically, ambulatory blood pressure monitoring could be used in clinical practice to screen for hypertension, to diagnose white-coat as opposed to sustained hypertension and to adjust antihypertensive treatment. According to the JNC VI guidelines [4], the indications for ambulatory monitoring also include hypotensive symptoms under antihypertensive drug treatment, episodic hypertension and autonomic dysfunction [18].

Screening for hypertension

Conventional sphygmomanometry, although it is prone to error [23–27], is easy and cheap to perform and is worldwide the standard technique used to screen for hypertension. However, the Riva Rocci/Korotkoff technique might soon lose its status as the standard method for non-invasive blood pressure measurement [53]. Indeed, in many European countries the mercury sphygmomanometer will be banned to protect the environment [53]. It will be replaced by fully automated and properly validated machines for blood pressure measurement [54], of which several are based on an oscillometric algorithm with data-storage and print-out facilities. In comparison with the Riva Rocci/Korotkoff approach and other techniques of stationary measurement of blood pressure, ambulatory blood pressure monitoring requires considerable investments in terms of equipment and training and can therefore not at present be recommended as a diagnostic instrument to screen for hypertension.

Diagnosis and treatment of white-coat hypertension

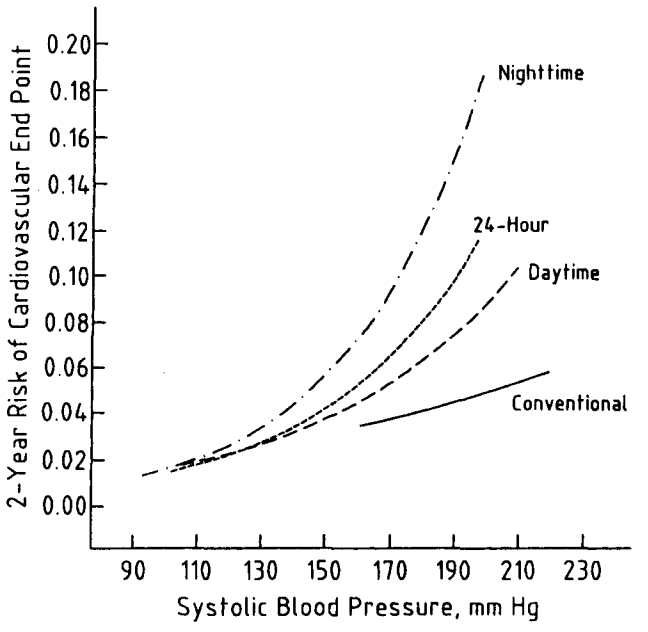
Diagnostic thresholds for ambulatory monitoring

The association between blood pressure and cardiovascular risk is continuous, without a threshold above which the risk suddenly increases [55,56]. However, clinical decisions must be based on diagnostic or operational thresholds. There is general consensus that the thresholds currently applicable for conventional sphygmomanometry [4,5] cannot be extrapolated and used for automated blood pressure measurements.

During the past 10 years diagnostic thresholds for ambulatory blood pressure monitoring of adults have gradually been developed. First, the distribution of the ambulatory blood pressure in normotensive subjects and untreated hypertensive patients who had initially been recruited and classified on the basis of their conventional blood pressures was studied [57–62]. Second, authors of various epidemiological studies investigated the distributions of the conventional and the ambulatory blood pressure for the population at large [2,63–76]. Third, several groups attempted to validate the preliminary thresholds for ambulatory monitoring by correlating the ambulatory blood pressure to left ventricular hypertrophy and other intermediary signs of target-organ damage [6–13] or to the incidence of cardiovascular morbidity (Fig. 2) and mortality [7,10,12–17].

On this basis it has been proposed [1–3] that, for adults, the upper limits of normotension in systolic/diastolic

Fig. 2



Systolic blood pressures obtained by conventional, 24 h, daytime and night-time measurement at randomization as predictors of the 2-year incidence of cardiovascular end points among the 393 patients of the Systolic Hypertension in Europe (Syst-Eur) Trial who were randomly allocated to placebo. The Cox models were standardized relative to female sex, mean age 69.6 years, no previous cardiovascular complications, no smoking and residence in western Europe. Reproduced with permission from [17].

Table 1 **Proposed thresholds for automated blood pressure measurements**

Blood pressure (mmHg)	95th percentiles[a]	Normotension[b]	Hypertension[c]
Ambulatory			
24 h	132/82	≤ 130/80	> 135/85
Daytime	138/87	≤ 135/85	> 140/90
Night-time	123/74	≤ 120/70	> 125/75
Self-recorded			
Morning	136/85	≤ 135/85	> 140/90
Evening	139/86	≤ 135/85	> 140/90
Morning and evening	137/85	≤ 135/85	> 140/90

[a]Mean value for the 95th percentiles in normotensive subjects in large-scale studies [1,2,156]. [b]Obtained by rounding downwards to the next value ending in 0 or 5. [c]Obtained by rounding upwards to the next value ending in 0 or 5.

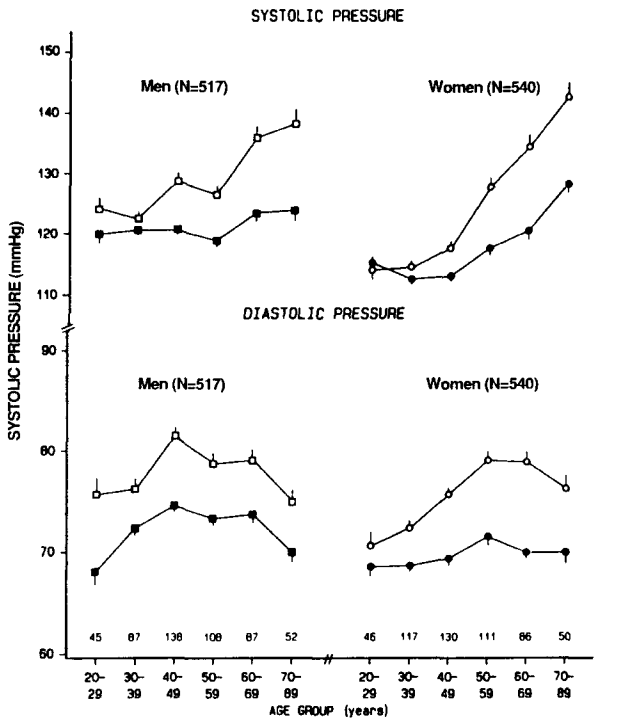
ambulatory measurements are 130/80 mmHg for the 24 h blood pressure and 135/85 and 120/70 mmHg for the daytime (from 1000–2000 h) and night-time (0000–0600) blood pressures, respectively (Table 1). On the other hand, hypertension is manifestly present if these values attain or exceed 135/85, 140/90 and 125/75 mmHg, respectively [1–3]. Some experts consider a daytime blood pressure below 130 mmHg systolic and below 80 mmHg diastolic as optimal [77]. Data in a large database currently support the proposed diagnostic thresholds in terms of their associations with left ventricular hypertrophy, other signs of target-organ damage and the incidence of cardiovascular complications (for review, see [17]). These limits are also in line with the recommendations of JNC VI [4] and those of many other national expert committees [19]. The diagnostic thresholds for ambulatory blood pressure monitoring of adults (Table 1), in the same way as those for conventional sphygmomanometry [4,5], do not account for sex and age. However, age is a stronger correlate of the conventional than it is of the ambulatory blood pressure in adults (Fig. 3) [64,66,76].

Some caution must be exercised regarding the above insofar as both clinic and ambulatory blood pressures are quantitatively related to cardiovascular risk and because the white-coat effect is itself not always reproducible. Moreover, the greater white-coat effect in older subjects, who constitute the majority of treated hypertensives [78], might reflect greater than normal arterial stiffness and hence a greater risk of adverse outcomes. Results of studies such as the Second Australian National Blood Pressure Study [79], which includes a substudy of the significance of white-coat hypertension in subjects aged 65–80 years in terms of outcome, may help to clarify these issues.

Ambulatory blood pressure monitoring for the diagnosis of hypertension

According to several sets of guidelines [4,5,19], ambulatory blood pressure monitoring is most clinically helpful and most commonly used for identifying patients with white-coat hypertension (isolated clinic hypertension [80]). The

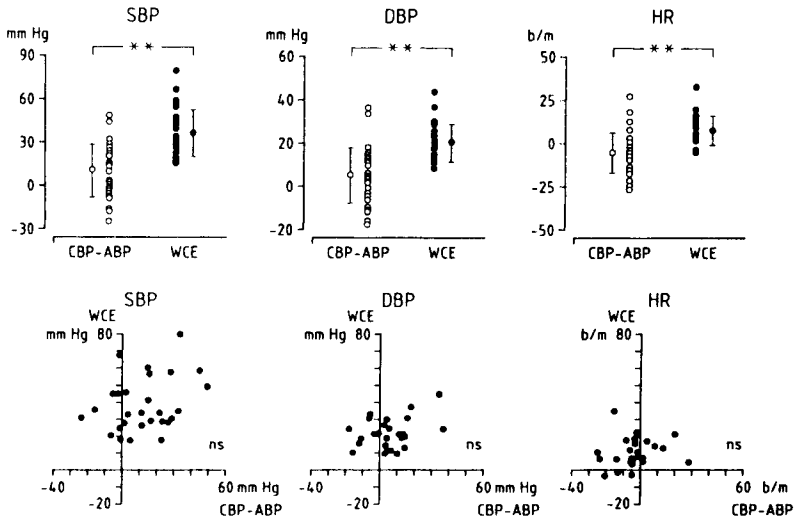
Fig. 3



Conventionally measured blood pressure (mean of five readings taken by a nurse in the participants' homes, open symbols) and 24 h ambulatory blood pressure (filled symbols) in a Belgian population study. Values are means ± SEM by 10-year age classes and sex. Reproduced with permission from [2].

prevalence of clinic or office hypertension in industrialized countries is nearly 15% of the adult population and can exceed 30% among those aged more than 70 years [78]. Among patients with clinic hypertension, the prevalence of white-coat hypertension varies from 15% [30,81] to 35% [60], depending on definitions. The diagnosis of hypertension most often implies life-long medical treatment. For patients with white-coat hypertension who have no signs of target-organ damage, antihypertensive drug treatment can be postponed or avoided by the use of ambulatory blood pressure monitoring [42]. In view of the high prevalence of white-coat hypertension, even if the clinic blood pressure is measured repeatedly during consecutive visits [62], ambulatory blood pressure monitoring, or an equivalent method for detecting the white-coat syndrome, should become part of the routine assessment of all patients with suspected hypertension, especially in those clinical centres, where sufficient resources and expertise to implement these techniques are available. Ambulatory blood pressure monitoring is especially indicated for patients with only a borderline elevation of their clinic blood pressure, among whom the prevalence of white-coat hypertension could be as high as 60–80%, as well as with young subjects, for whom life-long drug therapy might otherwise be inappropriately prescribed

Fig. 4



Comparison between the clinic minus daytime difference in blood pressure (CBP–ABP) and the increases in blood pressure and heart rate (HR) in 28 patients directly measured during the physician's visit [white-coat effect (WCE)]. Individual and average ± SEM group data are shown separately for systolic blood pressure (SBP), diastolic blood pressure (DBP) and HR. The within-subject correlations between CBP–ABP and WCE were not statistically significant. Reproduced with permission from reference [83].

and who may be penalized in matters relating to insurance and employment if they are misdiagnosed as hypertensive.

Originally, the white-coat syndrome was defined as a sympathetically mediated defence reaction against the observer measuring the conventional blood pressure [32]. In accord with this initial definition [32], the diagnosis of the white-coat phenomenon was based on simultaneous measurements of the intra-arterial blood pressure and the clinic blood pressure and required that rises both of blood pressure and of heart rate occurred during conventional sphygmomanometry. However, intra-arterial measurement of blood pressure cannot be used on a wide scale.

In a clinical context, the commonly used definition of white-coat hypertension is an elevation of the clinic blood pressure in the presence of a normal daytime ambulatory blood pressure [4]. However, this surrogate measurement of the white-coat effect only in part reflects the acute defence reaction and the white-coat phenomenon as they were originally described [32]. To a large extent the surrogate is also affected by other factors, such as measurement error and observer bias in the conventional blood pressure readings and the combined influences of lifestyle, medications, physical activity, psycho-emotional stress and other unspecific factors on the daytime ambulatory blood pressure [82]. This explains why the surrogate white-coat effect is also quantitatively different from and unrelated to the actual rise in blood pressure directly recorded by beat-to-beat blood pressure monitoring during a visit to a clinic (Fig. 4) [83].

Ambulatory blood pressure monitoring is itself not free of the white-coat syndrome. Indeed, the initial few measurements taken by the ambulatory recorder and the final readings constitute the 'white-coat window' reflecting the patient's attention to attaching and removing the monitoring device in a medical environment and are often abnormally elevated too [84]. Recent findings suggest that an elevation of the ambulatory blood pressure above 140 mmHg systolic and 90 mmHg diastolic during the first or last hour of monitoring makes it possible to diagnose the white-coat phenomenon independently of the clinic blood pressure and to identify a group of white-coat hypertensives with markedly elevated clinic blood pressures and higher than normal electrocardiographic Sokolow–Lyon [85] voltage indices [84].

How to deal with white-coat hypertension

A key issue for clinicians is knowing how to deal with so-called white-coat or isolated-office hypertensive patients. Whether white-coat hypertensive patients have a higher than normal risk of developing sustained hypertension remains debated [86,87]. There is a growing data base suggesting that, apart from the few cases misclassified during initial diagnosis, outcomes are better correlated to ambulatory blood pressure measurements than they are to clinic readings [7,10,12–17] and that white-coat hypertension is therefore genuinely a benign condition. In the Systolic Hypertension in Europe (Syst-Eur) Trial [17], to avoid problems with definitions and nomenclature [80], the white-coat effect was analysed as a continuous variable; the risk conferred by any level of conventional systolic

blood pressure at entry declined by nearly one-fifth for each 10 mmHg increase in the surrogate white-coat effect. The levels of the 24 h, daytime and night-time blood pressures (Fig. 2) which for subjects in the placebo group entailed a risk similar to that of a conventional systolic blood pressure of 160 mmHg were 142, 145, and 132 mmHg, respectively [17].

Antihypertensive medications lower the clinic, but not the ambulatory, blood pressure in patients with white-coat hypertension [88–91]. Nevertheless, the available evidence suggests that patients with white-coat hypertension should not be ignored. Other cardiovascular risk factors should be carefully addressed. If no cardiovascular complications are detected during diagnosis, treatment could be limited to further follow-up and the implementation of cardiovascular hygienic measures, such as regular exercise, reduction of excessive consumption of alcohol and sodium and loss of excess weight. Initial treatment should also account for other cardiovascular risk factors, such as smoking, hypercholesterolaemia and diabetes mellitus. Indeed, lower thresholds for initiating therapy are now recommended for patients with diabetes mellitus and renal disease [4,5]. During follow-up ambulatory blood pressure monitoring should be repeated at annual or 6-monthly intervals.

The non-pharmacological management of hypertension

Given the increasing importance of non-pharmacological approaches to the initial management of mild hypertension [4,5], there will be substantial numbers of hypertensives who remain without drug treatment, for whom it is important to evaluate cardiovascular risk attributable to blood pressure as accurately as possible. Just like with antihypertensive therapy, it will also be important to know whether a particular change in lifestyle is capable of materially improving 24 h control of blood pressure in hypertensive patients in general and whether this is in fact being achieved in the individual patient. Because the changes in blood pressure achievable by implementing changes in lifestyle exhibit large inter-individual variability, ambulatory blood pressure monitoring is the best available technique for assessing the effects of such non-pharmacological interventions [92,93].

The question regarding the efficacies of various changes in lifestyle is being addressed in a growing number of randomized controlled trials both with treated and with untreated hypertensive patients. Studies that have already yielded useful information on effects of lifestyle on ambulatory blood pressure have encompassed subacute or chronic effects of cigarette smoking [94], consumption of alcohol [95–97], control of weight [98–100], physical activity [99,101–103], consumption of caffeine [94,104,105], stress [57,92,106] and dietary factors, such as consumption of sodium [96,107,108], potassium [109,110], fat [111], fish [100] and fish oil [93,112,113] and complex dietary changes [100,112].

Few groups have reported direct comparisons of ambulatory blood pressure versus home and clinic blood pressures, although only the former can provide adequate data on 24 h and nocturnal control of blood pressure. The advantages and disadvantages of using ambulatory monitoring to assess effects of non-pharmacological interventions are essentially the same as those for other circumstances under which use of the technique is recommended. However, current machines are not suitable for use during vigorous physical activity [22]. Interference with sleep patterns can also lead to overestimates of usual night-time blood pressures [114–116]. All these issues notwithstanding, the more comprehensive information provided by ambulatory monitoring makes its use in lifestyle intervention studies in which blood pressure is a primary end point virtually mandatory before population-based advice is given.

Diagnosis and management of treatment-resistant hypertension

Ambulatory blood pressure monitoring is superior to conventional sphygmomanometry not only in selecting patients for antihypertensive drug treatment but also in assessing the effects of such treatments. Results of two studies [9,11] showed that changes in ambulatory blood pressure were correlated more closely to regression of left ventricular hypertrophy than were the changes in the conventional blood pressure. Ambulatory monitoring is therefore an excellent technique for evaluating treatment-resistant hypertension.

The current guidelines do not provide recommendations on the frequency with which ambulatory blood pressure monitoring should be repeated for hypertensive patients under medical treatment. If the initial evaluation demonstrates the absence of a white-coat phenomenon, then periodic clinic measurements may be adequate. Just like for patients with white-coat hypertension, in clinical centres where sufficient resources can be allocated, an interval of 1–2 years between consecutive recordings seems reasonable, unless there is a special indication for more frequent recordings. The treatment should lower ambulatory blood pressure to below the thresholds applied for diagnosing sustained hypertension.

The cost-effectiveness of using ambulatory blood pressure monitoring as an accessory to conventional sphygmomanometry needs further research. A survey of a general medical practice in Michigan demonstrated that, on the basis of the prevailing costs of antihypertensive drug treatment and the prevalence of white-coat hypertension the break-even cost for performing ambulatory blood pressure monitoring would be £118 [117]. However, in Europe [42],

ambulatory blood pressure monitoring does not reduce the short-term costs of antihypertensive treatment. Whether these conclusions [41,117] would still be valid in the long-run, especially after accounting for morbidity and mortality, or in different settings or countries [118] still remains to be elucidated.

Diagnosis of nocturnal hypertension

Ambulatory blood pressure monitoring makes blood pressure measurement during sleep possible. The hypothesis that non-dipping is associated with greater than normal cardiovascular risk [119] is not yet generally accepted [120], although evidence that the night-time blood pressure provides important prognostic information is accumulating. Poor reproducibility of the dipping status [65] and the use of varying definitions of non-dipping [7,74] have contributed to the controversy.

To avoid the use of arbitrary thresholds, the Syst-Eur investigators analysed the night : day ratio of blood pressure as a continuous variable [17]. They found that the relative hazard rates associated with a 10 mmHg increase in the 24 h systolic blood pressure and with a 10% higher night : day ratio of systolic blood pressure were 1.23 (95% confidence interval 1.03–1.46, $P = 0.02$) and 1.41 (1.03–1.94; $P = 0.03$), respectively. Thus, the hypothesis that there is an inverse association between cardiovascular risk and dipping of blood pressure at night was confirmed valid [119]. In addition, the night-time blood pressure behaved as a more consistent predictor of major end points than did the daytime blood pressure. The variability due to physical activity and psycho-emotional stress might weaken the predictive power of the daytime blood pressure, whereas the greater uniformity resulting from sleeping might help to demonstrate correlations to the night-time blood pressure. The observation that the mean ± SD within-subject coefficient of variation was significantly smaller for the night-time than it was for the daytime blood pressure (8.7 ± 3.6 versus 10.4 ± 3.3%, $P < 0.0001$) is in line with this hypothesis [17]. Another explanation for the close correlation between cardiovascular risk and the night-time blood pressure could be that they are linked to a common pathophysiological mechanism, such as a rise in sympathetic tone [121] or renal dysfunction necessitating a higher night-time blood pressure in order to sustain natriuresis [122].

Patients with secondary hypertension usually have considerably elevated blood pressures, while their diurnal profiles are often flattened or even inverted [123–126]. Even though this is not a very sensitive test, when ambulatory monitoring reveals severe sustained hypertension, especially in the presence of a non-dipping nocturnal blood pressure, the possibility of secondary hypertension should be considered.

Management of hypertension in special groups

Old patients

In the Syst-Eur trial systolic blood pressure was on average 22.0 mmHg higher ($P < 0.001$) with conventional than it was with daytime ambulatory measurement. The corresponding mean ± 2SD interval of this excess ranged from −8.3 to +52.3 mmHg [17]. These results illustrate that conventional sphygmomanometry, even when it is repeated during different out-patient visits, can lead to considerable overestimation of the systolic blood pressure and probably also to excessive treatment of systolic hypertension.

The Syst-Eur findings also demonstrated that the systolic ambulatory blood pressure in untreated old patients with isolated systolic hypertension predicted cardiovascular risk over and above the conventional blood pressure [17]. Active treatment weakened this relationship to a level that was no longer significant. For subjects in the placebo group the risk conferred by any level of conventional systolic blood pressure at entry declined by nearly one fifth for each 10 mmHg decrease in the daytime systolic blood pressure and for each 10 mmHg increase in the white-coat effect. For old patients with white-coat hypertension, just like for young patients with this condition [88–91], active treatment lowers the clinic, but not the ambulatory, blood pressure. White-coat hypertension is common among the elderly and the diagnosis of this condition by ambulatory monitoring could allow a reduction in dose or even a withdrawal of antihypertensive medication.

During ambulatory monitoring diurnal blood pressures of some old hypertensive patients exhibit striking variability, with periods of hypotension interspersed with hypertension. It is important to identify this pattern, which is often indicative of autonomic failure [127], so that treatment can be tailored to take account of the fluctuations in blood pressure. Furthermore, in general, old patients are prone to developing hypotension, which can be postural or postprandial [128,129] in nature, which can be caused by dysfunction of baroreceptors or autonomic failure [127], or could be the consequence of the greater than normal susceptibility of the elderly to the adverse effects of blood-pressure-lowering drugs. The identification of symptomatic hypotension constitutes a privileged indication for the clinical use of ambulatory monitoring of blood pressure in the elderly [130].

Ambulatory blood pressure monitoring in pregnancy

Several devices for ambulatory monitoring have been validated specifically for pregnant women [49,50]. Just like for women in the non-pregnant state, the main indication for ambulatory monitoring during pregnancy is the measurement of the white-coat effect. Its recognition is important so that pregnant women are not administered antihypertensive drugs unnecessarily or excessively.

Normal values for ambulatory blood pressure for the population of pregnant women are available [131,132] and the changes in blood pressure which occur during the trimesters of pregnancy and the post-partum period have been defined [132]. The evidence that ambulatory blood pressure monitoring can predict pre-eclamptic toxaemia is not yet conclusive [133–135]. On the other hand, hypertension during pregnancy, diagnosed using ambulatory monitoring, has been shown to be associated with birth of infants weighing less than do those born to normotensive women [136].

Self-measurement as an alternative to ambulatory monitoring

Regardless of any cost–benefit consideration, the investment in equipment and software still prevents the large-scale implementation in most countries of ambulatory blood pressure monitoring in primary care, the first line in diagnosing and treating hypertension. However, the development of cheap, automated and properly validated devices stimulated the clinical application of the self-recording of blood pressure [137–141]. In the near future, the latter technique [18,142,143] could provide a valid and less expensive alternative to ambulatory blood pressure monitoring. Oscillometry is likely to prevail as the preferred technique both for ambulatory monitoring and for automated self-measurement [22,54].

Advantages of the self-measured blood pressure

Variation in blood pressure throughout the whole day can be monitored only by ambulatory measurement, but several advantages of the latter approach can also be obtained with self-measurement [144,145]. The greater number of readings [140,146], which can be obtained in a practical way, and the absence of the white-coat effect [39,147] contribute to a better diagnostic accuracy than that with conventional sphygmomanometry [18,148,149]. Furthermore, self-measurement of blood pressure has been shown to increase compliance to prescriptions of drugs [150,151] and to reduce the number of visits to a clinic required for the diagnosis and the treatment of hypertension [152–154]. If automated devices are used [140], the self-recorded blood pressure is also free of observer bias. However, selection by the patient of more favourable readings could still be a problem.

Diagnostic thresholds for automated self-measurement

The widespread clinical use of self-measurement is still limited by the lack of a generally accepted reference frame for initiating and adjusting antihypertensive treatment. However, the strategy for determining diagnostic thresholds for ambulatory blood pressure monitoring developed over the last decade could serve as a template. Furthermore, in view of the similarity between the measurement techniques as well as the conditions under which these measurements take place, the diagnostic thresholds for the daytime ambulatory blood pressure and the self-recorded blood pressure are likely to be of the same order of magnitude.

A recent meta-analysis of summary statistics [155] demonstrated that the self-recorded blood pressure averaged 115/71 mmHg for normotensive persons and 119/74 mmHg for untreated subjects not selected on the basis of their blood pressures. The thresholds for the self-recorded blood pressures in normotensive people determined from 95th percentiles (135/86 mmHg) or by adding 2SD to the means (137/89 mmHg) were concordant to within 2/3 mmHg. Furthermore, in an international data base of self-recorded blood pressures [156], the 95th percentile values for 2401 normotensive persons were 136/85 mmHg for the measurements taken in the morning, 139/86 mm Hg for the measurements obtained in the evening and 137/85 mmHg for the self-recorded blood pressure regardless of the time of day (Table 1). This meta-analysis of data on individual patients indicated that a self-recorded blood pressure above 137 mmHg systolic or 85 mmHg diastolic should be considered hypertensive. These thresholds are in close agreement with those for the daytime ambulatory blood pressure (Table 1) and with other proposals for self-recorded measurements [70,155,157–159].

Up to now, few studies with the goal of validating self-recorded blood pressure measurements in terms of cardiovascular complications have been published. In a prospective Japanese population study, the self-recorded blood pressure was a better predictor of subsequent mortality than was the screening blood pressure [160]. In the Treatment of Hypertension According to Home or Office Blood Pressure (THOP) Trial [161] it is currently being investigating whether antihypertensive treatment guided by the self-measured blood pressure is more beneficial and cost-effective than is treatment based on conventional sphygmomanometry. In this trial all patients will also be undergoing ambulatory monitoring at baseline and 6 and 12 months after randomization. On 31 August 1999, 253 of the projected 400 patients had been randomized.

Summary and conclusions

The Riva Rocci/Korotkoff technique [23], although it is prone to error, is easy and cheap to perform and remains worldwide the standard procedure for measuring blood pressure. Ambulatory blood pressure monitoring should be performed only with properly validated devices as an accessory to conventional blood pressure measurement. Ambulatory blood pressure recording requires considerable investment in equipment and training and cannot be recommended for purposes of screening.

Ambulatory blood pressure monitoring is most helpful in identifying patients with white-coat hypertension (isolated clinic hypertension [80]), which is arbitrarily defined as a

clinic blood pressure of more than 140 mmHg systolic or 90 mmHg diastolic in the presence of a daytime ambulatory blood pressure below 135 mmHg systolic and 85 mmHg diastolic. Some experts consider a daytime blood pressure below 130 mmHg systolic and 80 mmHg diastolic optimal [77]. Whether white-coat hypertension predisposes subjects to sustained hypertension remains debated. However, outcomes are better correlated to the ambulatory blood pressure than they are to the conventional blood pressure. Antihypertensive medications lower the clinic blood pressure, but not the ambulatory blood pressure, in patients with white-coat hypertension and also do not improve their prognosis [7]. Nevertheless, white-coat hypertension should not be left unattended. In cases with no previous cardiovascular complications, treatment could be limited to follow-up and to hygienic measures, which should also account for risk factors other than hypertension.

Ambulatory blood pressure monitoring is superior to conventional blood pressure measurement not only in selecting patients for antihypertensive drug treatment but also in assessing the effects both of non-pharmacological and of pharmacological therapy. The treatment should reduce ambulatory blood pressure to below the thresholds applied for diagnosing sustained hypertension. Ambulatory blood pressure monitoring makes the diagnosis and treatment of nocturnal hypertension possible and is especially indicated for patients with borderline hypertension, the elderly, pregnant women, patients with treatment-resistant hypertension and patients with symptoms suggestive of hypotension. In centres with sufficient financial resources, ambulatory blood pressure monitoring should become part of the routine assessment of patients with clinic hypertension. For patients with white-coat hypertension ambulatory blood pressure monitoring should be repeated at annual or 6-monthly intervals. Variation in blood pressure throughout the whole day can be monitored only by ambulatory monitoring, but several advantages of the latter technique can also be obtained by self-measurement of blood pressure, which is a less expensive method that is probably better suited to primary practice and use in developing countries.

In conclusion, ambulatory blood pressure monitoring or equivalent methods for tracing the white-coat effect should become part of the routine diagnostic and therapeutic procedures for dealing with treated and untreated patients with elevated clinic blood pressures. Long-term outcome trials with designs similar to that of the APTH trial [42] should better establish the advantage of further integrating ambulatory blood pressure monitoring as an accessory to conventional sphygmomanometry into the routine care of hypertensive patients and should provide more definite information on the long-term cost-effectiveness. Because such trials are not likely to be funded by the pharmaceutical industry, governments and health insurance companies should take responsibility in this regard.

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