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Modern approaches to blood pressure measurement

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Abstract

***Background*—Blood pressure (BP) is usually measured by conventional sphygmomanometry. Although apparently simple, this procedure is fraught with many potential sources of error. This review focuses on two alternative techniques of BP measurement: ambulatory monitoring and self measurement.**

***Review*—BP values obtained by ambulatory monitoring or self measurement are characterised by high reproducibility, are not subject to digit preference or observer bias, and minimise the transient rise of the blood pressure in response to the surroundings of the clinic or the presence of the observer, the so called white coat effect. For ambulatory monitoring, the upper limits of systolic/diastolic normotension in adults include 130/80 mm Hg for the 24 hour BP and 135/85 and 120/70 mm Hg for the daytime BP and night time BP, respectively. For the the self measured BP these thresholds include 135/85 mm Hg. Automated BP measurement is most useful to identify patients with white coat hypertension. Whether or not white coat hypertension predisposes to sustained hypertension remains debated. However, outcome is better correlated with the ambulatory BP than with the conventional BP. In patients with white coat hypertension, antihypertensive drugs lower the BP in the clinic, but not the ambulatory BP, and also do not improve prognosis. Ambulatory BP monitoring is also better than conventional BP measurement in assessing the effects of treatment. Ambulatory BP monitoring is necessary to diagnose nocturnal hypertension and is especially indicated in patients with borderline hypertension, elderly patients, pregnant women, patients with treatment resistant hypertension, and also in patients with symptoms suggestive of hypotension.**

***Conclusions*—The newer techniques of BP measurement are now well established in clinical research, for diagnosis in clinical practice, and will increasingly make their appearance in occupational and environmental medicine.**

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Keywords: ambulatory blood pressure; self measurement; white coat hypertension

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Blood pressure measurement, apparently a simple procedure, is of great relevance to occupational and environmental medicine. Some pollutants—such as lead[1–3] or cadmium,[4–6]—at exposure concentrations encountered at the workplace or in the environment, are suspected to increase blood pressure and to cause hypertension. Other studies showed that job strain, defined as high psychosocial demand and low decision latitude, correlated significantly and positively with hypertension.[7 8] Furthermore, the medical examination of the work force, at the time of first employment or later at regular follow up intervals, commonly involves a measurement of blood pressure. Some jobs with much responsibility for the security of other people, require that from a cardiovascular perspective the applicant or employee is in good health and normotensive. Specialised hypertension clinics, therefore, often have to deal with referrals from occupational medical services to confirm or to refute the diagnosis of hypertension.

In most circumstances blood pressure is measured by conventional sphygmomanometry and by auscultation of the Korotkoff sounds.[9] The past two decades have witnessed a growing awareness of the imperfection of the Korotkoff method. Newer techniques, such as ambulatory blood pressure monitoring[10–12] and the self measurement of blood pressure[13] are gradually gaining wide acceptance in clinical medicine to overcome some of the limitations of conventional sphygmomanometry. The goal of this review article is to put these newer approaches to blood pressure measurement into perspective.

Limitations of conventional sphygmomanometry

The measurement of blood pressure in clinical practice is dependent on the accurate transmission and interpretation of the arterial pulse wave and the Korotkoff sounds. The procedure is fraught with potential sources of error, which may arise in the subject, the observer, the sphygmomanometer, or in the overall application of the technique.[14 15] Even if all possible precautions are taken, the accuracy of

non-invasive blood pressure measurement, in comparison with intra-arterial readings, remains imperfect.[16 17] The Korotkoff method tends to produce values for systolic blood pressure that are lower than the intra-arterial pressure, whereas the reverse is true for diastolic blood pressure without obvious superiority of phase V over phase IV.[17]

Systematic error in the sphygmomanometric measurement of blood pressure may be caused by lack of mental concentration, deteriorating auditory acuity, or failure to accurately interpret the Korotkoff sounds.[18] 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.[18 19] Observer bias is the practice whereby the observer simply adjusts the blood pressure reading to meet a preconceived idea of what it should be.[18 20] Observer prejudice is most likely to occur when an arbitrary division line is applied to diagnose hypertension, to recruit patients, or to adjust treatment.[20] Moreover, the presence of an observer—such as a nurse or a doctor—may arouse the patient and increase the blood pressure.[21–25] This so called white coat phenomenon may lead to an overestimation of blood pressure, and hence to the artifactual diagnosis of hypertension. In patients with white coat hypertension, the seemingly increased blood pressure is not sustained in the absence of the observer.[21–25]

Another major drawback of conventional sphygmomanometry stems from the fact that blood pressure is highly variable,[26] and as originally shown by researchers from Oxford,[27] is characterised by large diurnal fluctuations.[28] Single measurements or multiple readings taken by an auscultating observer at one or even several times through the day, reflect a subject's true blood pressure only to a minor extent. It is ironic that influential studies (for a review see Staessen *et al*[3]), which are viewed to support the hypothesis of a positive relation between hypertension and environmental lead exposure, based their conclusions on blood pressure measurements at one examination or on a single blood pressure reading.[29 30] In other reports[3] the blood pressure was measured in a non-standardised fashion or in exceptional circumstances, such as labour in pregnant women.[31] The planners of the 3rd national health and nutrition examination survey (1988–94)[32] recognised this problem; in people aged 17 and over the seated blood pressure was measured three times at home and three times at mobile examination clinics.

A meta-analysis of nine prospective observational studies[33] also highlighted the issue of regression dilution bias in assessing the correlations between disease outcomes and a risk factor—such as blood pressure. If the level is only measured on a single occasion, the results are biased by random fluctuation, so that the true association between a possible disease outcome and the usual blood pressure level (a person's long term mean blood pressure) is seriousy underestimated.[33 34] After correction for regression dilution bias,[33] the slope of the relation (the relative risk for a given rise in blood pressure) steepens (fig 1). A reverse phenomenon may occur when in regression analysis blood pressure is the dependent variable and plotted, for instance, against age (fig 1) or body mass index.[35]

Ambulatory blood pressure measurement

Ambulatory blood pressure monitoring makes it possible to record the blood pressure throughout the whole day in patients engaged in their normal activities and to provide within 24 hours a reliable estimate of their blood pressure.[36] To collect the same information, conventional measurements must be repeated at intervals of a few weeks.[37] Furthermore, the ambulatory blood pressure is characterised by high reproducibility,[38] is not subject to digit preference and observer bias,[20] and avoids the transient rise of a patient's blood pressure in response to the surroundings of the clinic or

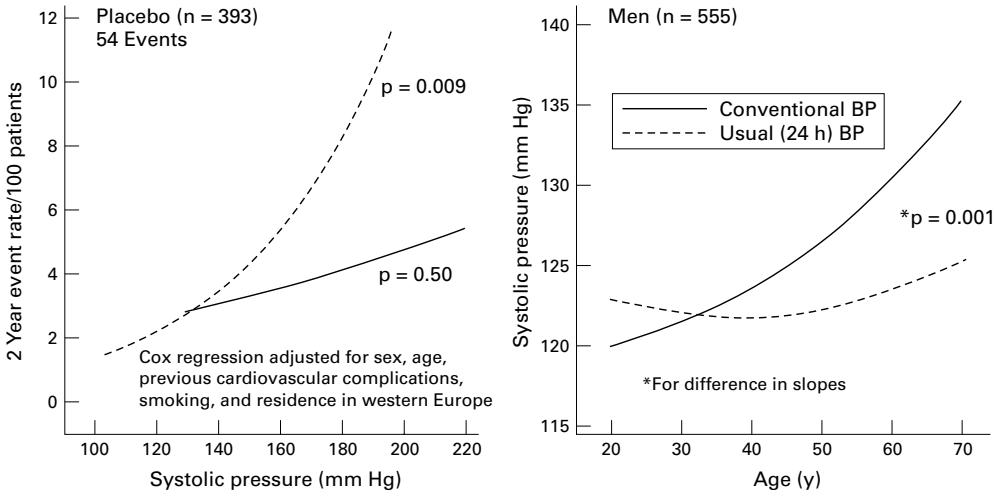

Figure 1 Plots involving the conventional and the usual blood pressures measured in the same people in each of two studies.[35 47] The conventional blood pressure was the mean of two[47] or five[35] blood pressure readings at two separate examinations and the usual blood pressure was estimated by 24 hour ambulatory monitoring. If blood pressure is the independent variable, the slope of the relation is steeper for the usual than for the conventional blood pressure (left panel; regression dilution bias[33]; data from the placebo group[47]); the opposite occurs when blood pressure is the dependent variable (right panel; data from[35]).

Table 1 The 95th percentiles as the upper limits of the distribution of the ambulatory blood pressure in normotensive subjects

	IDB	*AIB-S*	*Bel-PS*	*Jap-PS*	*Dan-PS*	*It-PS*	*All*
References	45.62	44	56	48.49	57	58	
Subjects:							
All	7320	815	1057	705	352	1438	11687
Normotensive subjects*	3188†	807	729	324‡	238‡	1402	5286
Mean (range) age (y)	48 (10–99)	36 (17–80)	50 (20–88)	59 (20–79)	49 (20–79)	46 (25–64)	48 (10–99)
Systolic pressure (mm Hg):							
Conventional	140	136	136	136	137	137	137
Whole day	134	131	129	134	136	128	132
Daytime	141	138	137	138	139	134	138
Night time	128	120	121	128	122	121	123
Diastolic pressure (mm Hg):							
Clinic	87	88	86	86	89	89	88
Whole day	82	82	80	79	86	82	82
Daytime	88	89	88	83	88	88	87
Night time	77	72	72	74	77	74	74

*95th percentiles were determined in normotensive subjects, with conventional blood pressure lower than 140 mm Hg systolic and 90 mm Hg diastolic.
†This group excludes participants of the Allied Irish Bank Study and the Belgian population study, who were analysed separately.
‡For the Japanese and Danish studies, the authors provided the 95th percentiles from the databases described in references 49 and 57, respectively.
IDB=International database; AIB-S=Allied Irish Bank study; Bel-PS, Jap-PS, Dan-PS, It-PS=Belgian, Japanese, Danish, and Italian population studies, respectively.

the presence of the observer,[24] the so called white coat effect.[22 39]

DEFINITION OF DIAGNOSTIC THRESHOLDS FOR AMBULATORY BLOOD PRESSURE MONITORING

The association between blood pressure and cardiovascular risk is continuous without a threshold above which the risk suddenly increases.[40 41] However, clinical decisions must be based on diagnostic or operational thresholds. For ambulatory blood pressure monitoring, initially, these thresholds were largely based on the distribution of the ambulatory blood pressure in normotensive subjects and untreated hypertensive patients.

Firstly, several smaller studies described the ambulatory blood pressure in healthy subjects or in patients referred to specialised clinics to exclude the diagnosis of hypertension (for a review see Staessen *et al*[42]). In these reports the mean systolic blood pressure over the whole day ranged from 111 to 124 mm Hg; the daytime averages ranged from 115 to 128 mm Hg and the night time means from 99 to 111 mm Hg; the corresponding ranges for the diastolic blood pressure embraced 59 and 79 mm Hg, 63 and 85 mm Hg, and 51 and 70 mm Hg, respectively.[42] Further epidemiological studies in well defined professional groups,[43 44] in normotensive and hypertensive subjects,[42 45–47] and in the population at large[35 48–61] subsequently led to various proposals for normality of blood pressure on ambulatory measurement.

Table 2 Proposed thresholds for automated blood pressure measurements

	*95th percentiles**	*Normotension†*	*Hypertension‡*
Ambulatory blood pressure:			
24 h (mm Hg)	132/82*	⩽130/80	>135/85
Daytime (mm Hg)	138/87*	⩽135/85	>140/90
Night time (mm Hg)	123/74*	⩽120/70	>125/75
Self recorded blood pressure:			
Morning (mm Hg)	136/85	⩽135/85	>140/90
Evening (mm Hg)	139/86	⩽135/85	>140/90
Morning and evening (mm Hg)	137/85	⩽135/85	>140/90

*Mean value for the 95th percentiles in normotensive subjects (see table 1).
†Obtained by rounding downward to the next blood pressure value ending in 0 or 5.
‡Obtained by rounding upward to the next value ending in 0 or 5.

The most prominent feature of the larger studies on ambulatory monitoring[42 44 45 49 51 52 59 62–64] is their striking concordance in the reported statistics, be it the mean plus two SDs (for a review see Staessen *et al*[65]) or the 95th percentile (table 1). Averaging the 95th percentiles in the normotensive subjects and rounding the resulting boundaries downwards or upwards to the nearest value ending in 0 or 5, may produce working definitions of normality for ambulatory monitoring, which can be easily remembered (table 2). The upper limits of normotension, calculated by rounding downwards, include 130/80 mm Hg for the 24 hour blood pressure and 135/85 mm Hg and 120/70 mm Hg for the daytime and night time blood pressures, respectively. Abnormality, obtained by rounding upwards, corresponds with blood pressures exceeding 135/85, 140/90, and 125/75 mm Hg. These preliminary threshold values did not account for sex and age. However, the boundaries currently in use for normotension and hypertension on conventional blood pressure measurement and jointly endorsed by the World Health Organisation/International Society for Hypertension (WHO/ISH)[66] and the 6th report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI),[67]—namely, 140 mm Hg systolic and 90 mm Hg diastolic—are also uniformly applicable to men and women and across all ages. Moreover, age correlates more strongly with the conventional than with the ambulatory blood pressure (fig 1, right panel).[35 49 61]

VALIDATION OF THE DIAGNOSTIC THRESHOLDS IN TERMS OF LEFT VENTRICULAR HYPERTROPHY

The diagnostic thresholds proposed in table 1 are supported by the prospective study of Verdecchia *et al*.[68] Indeed, the boundaries proposed for the daytime blood pressure approximate to the cut off values of 136/87 mm Hg in men and 131/86 mm Hg in women, below which the incidence of cardiovascular events

was the same in patients with white coat hypertension and normotensive subjects.[68]

Devereux *et al*[69] contrasted the ambulatory measurements in normotensive subjects with normal left ventricular geometry with those in patients with concentric left ventricular hypertrophy, the morphological pattern associated with the worst prognosis.[70] These investigators suggested that in awake adult men and women ambulatory blood pressures below 139/86 mm Hg may be considered normal, whereas values over 145/95 mm Hg should be viewed as pathological.[69] Along similar lines, Gosse *et al*[71] found that the left ventricular mass index increased with higher daytime blood pressure, but not with a larger white coat effect defined as the difference between the clinic and the daytime blood pressure. In the study of Gosse *et al*[71] left ventricular mass index was on average not increased (125 g/m^2) in the patients in the bottom quartile of the daytime blood pressure, in whom during the day the systolic blood pressure ranged up to 133 mm Hg and the diastolic up to 89 mm Hg.

VALIDATION OF THE DIAGNOSTIC THRESHOLDS FOR MORBIDITY AND MORTALITY

Perloff *et al* started the validation of ambulatory blood pressure monitoring in terms of hard cardiovascular end points.[72 73] These investigators used the patient activated Remler M-2000 recorder (Remler Corporation, San Fransisco, CA, USA). They showed for the first time that the portion of the daytime ambulatory blood pressure, which was not already explained by systolic or diastolic clinic blood pressure, could discriminate high risk from low risk hypertensive patients.[72] These results obtained in 1076 hypertensive patients by life table analysis were later confirmed by Cox regression in a subgroup of 761 patients, who were untreated at baseline.[73] With stratification for previous cardiovascular complications and with cumulative adjustments for clinic blood pressure, sex, age, electrocardiographic left ventricular hypertrophy, hypertensive retinopathy, and subsequent antihypertensive drug treatment, a higher systolic ambulatory blood pressure was still a harbinger of a worse cardiovascular outcome.[73] Furthermore, a smaller study of 137 newly referred hypertensive patients showed that blood pressure, when measured intra-arterially over 24 hours, significantly increased the prognostic accuracy of conventional blood pressure readings.[74] A recent report from the same centre included 479 patients who underwent 24 hour intra-arterial blood pressure monitoring and were followed up for an average of 9.1 years.[75] White coat hypertension, defined as a clinic systolic blood pressure of 140–180 mm Hg and a 24 hour blood pressure of less than 140 mm Hg systolic and 90 mm Hg diastolic, was present in 126 patients; compared with the patients with sustained hypertension (n=353), white coat hypertensive patients had a 71% lower risk (95% confidence interval (95% CI) 10%–91%; p=0.04) of experiencing cardiovascular events.[75]

Verdecchia *et al* followed up (mean 3.2 years) 1187 subjects with essential hypertension and 205 healthy normotensive control subjects, who all underwent baseline (off treatment) 24 hour non-invasive ambulatory blood pressure monitoring.[68] In the hypertensive patients the prevalence of white coat hypertension, defined as a mean daytime blood pressure lower than 136/87 mm Hg in men and 131/86 mm Hg in women, was 19.2%. After adjustment for traditional markers of cardiovascular risk, morbidity did not differ between the normotensive subjects and the group with white coat hypertension (p=0.83).[68] Recently, Ohkubo *et al* found 1542 residents of a rural Japanese community, aged 40 years and over, in that their 24 hour systolic and diastolic blood pressures were significantly and curvilinearly correlated with total mortality.[76] This second order relation persisted after cumulative adjustments for sex, age, smoking, use of antihypertensive medication at baseline and history of cardiovascular disease, diabetes, and hypercholesterolaemia. It also persisted after further adjustment for the conventional blood pressure at baseline and if the non-cardiovascular deaths were excluded from the analysis.[77] Furthermore, Redon *et al* studied patients with refractory hypertension, defined as a diastolic blood pressure of more than 100 mm Hg, while taking three or more antihypertensive drugs.[78] Patients were classified into three groups according to their daytime ambulatory blood pressure; those in the lowest tertile (<88 mm Hg) had a significantly lower rate of morbidity over the next 4 years than those in the middle (88–97 mm Hg) or highest (>97 mm Hg) tertiles. No differences in clinic blood pressure were found between these three groups either at baseline or at the time of the last evaluation.[78]

In a substudy[47 79 80] to the double blind placebo controlled systolic hypertension in Europe (Syst-Eur) trial,[81 82] the prognostic significance of conventional and ambulatory blood pressure measurement was compared in older patients with isolated systolic hypertension. The conventional blood pressure at randomisation was the mean of six readings (two measurements in the sitting position at three visits 1 month apart). The baseline ambulatory blood pressure was recorded with a non-invasive intermittent technique. Older (⩾60 years) patients whose untreated blood pressure on conventional measurement at baseline was 160–219 mm Hg systolic and less than 95 mm Hg diastolic, were randomised to nitrendipine (10–40 mg/day) with the possible addition of enalapril (5–20 mg/day) or hydrochlorothiazide (12.5–25 mg/day) or both, or to matching placebos.[81] With cumulative adjustments applied for sex, age, previous cardiovascular complications, smoking, and residence in western Europe,[83] higher systolic blood pressure at randomisation predicted a worse prognosis (fig 2), whereas the association between diastolic blood pressure and outcome was not significant.[47] In the placebo group (n=393), the 24 hour, daytime (1000 to 2000), and night time (0000 to 0600) systolic ambulatory blood pressure predicted the incidence of cardiovascular complications even after

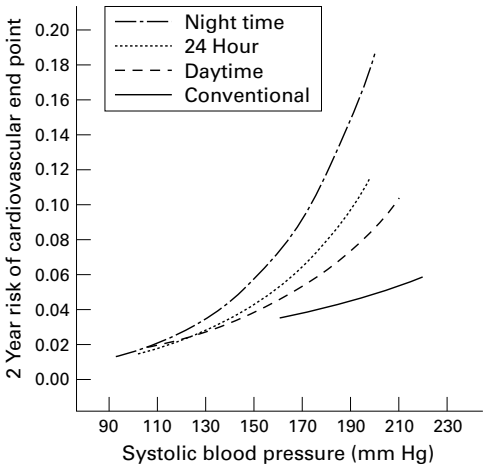

Figure 2 Systolic blood pressure on conventional, 24 hour, daytime, and night time measurement at randomisation as predictors of the 2 year incidence of cardiovascular end points in the 393 patients of the systolic hypertension in Europe (Syst-Eur) trial randomised to placebo. The Cox's models were standardised to female sex, 69.6 years (mean age), no previous cardiovascular complications, non-smoking, and residence in western Europe. Reproduced with permission from Staessen et al.[47]

further adjustment for the conventional blood pressure.[47] At randomisation, the cardiovascular risk conferred by a conventional systolic blood pressure of 160 mm Hg was similar to that associated with a 24 hour, daytime, or night time systolic blood pressure of 142 mm Hg, 145 mm Hg, or 132 mm Hg, respectively (fig 2).[47] In the active treatment group (n=415), systolic blood pressure at randomisation did not significantly predict cardiovascular risk, regardless of the technique of blood pressure measurement. This finding confirmed that active treatment had reduced the excess risk conferred by hypertension.

Diagnosis and treatment of white coat hypertension

AMBULATORY BLOOD PRESSURE MONITORING FOR THE DIAGNOSIS OF HYPERTENSION

According to several sets of guidelines,[66 67 84] ambulatory blood pressure monitoring is most clinically helpful and most commonly used to identify patients with white coat hypertension (table 3). The prevalence of clinic hypertension in industrialised countries is nearly 15% of the adult population and may exceed 30% in those older than 70.[85] Among patients with clinic hypertension, the prevalence of white coat hypertension varies from 15%[22 86] to 35%,[45] depending on definitions.

The diagnosis of hypertension most often implies lifelong medical treatment. In patients with white coat hypertension who have no signs of target organ damage, antihypertensive drug treatment may be postponed or avoided by the use of ambulatory blood pressure monitoring.[87] In view of the high prevalence of white coat hypertension, even if the clinic blood pressure is measured repeatedly at consecutive visits,[47] ambulatory blood pressure monitoring, or an equivalent method of detecting the white coat syndrome, should become part of the routine investigation of all patients with suspected hypertension, in particular in those clinical centres, where sufficient resources and expertise are available to implement these techniques. Ambulatory blood pressure monitoring is especially indicated in patients with only a borderline increase of their clinic blood pressure in whom the prevalence of white coat hypertension may be as high as 60%–80%, as well as in young subjects in whom lifelong drug treatment may be inappropriately prescribed and who may be penalised for insurance or employment if misdiagnosed as hypertensive (table 3).

Ambulatory blood pressure monitoring is itself not completely free from the white coat syndrome. Indeed, the initial few measurements on the ambulatory recorder and the final readings constitute the white coat window, reflect the patient's attention to attaching and removing the monitoring device in a medical environment and are often abnormally increased.[88] Recent findings suggest that an increase in the ambulatory blood pressure above 140 mm Hg systolic and 90 mm Hg diastolic in the first or last hour of monitoring makes it possible to diagnose the white coat phenomenon independent of the clinic blood pressure and to identify a white coat hypertensive group with markedly increased clinic blood pressures and higher electrocardiographic Solokow-Lyon[89] voltage indexes.[88]

Table 3 Indications for ambulatory blood pressure monitoring

Privileged indications
Identification and follow up of patients with white coat hypertension
Young patients*
Patients with borderline clinic hypertension
Management of treatment resistant hypertension
Diagnosis of nocturnal hypertension
Episodic hypertension
Management of hypertension in special groups
Elderly
Pregnant women
Suspicion of hypotension or autonomic dysfunction

*In particular patients undergoing a medical check up when applying for a job or insurance policy.

IS WHITE COAT HYPERTENSION REALLY INNOCENT?

A key issue for clinicians is to know how to deal with so called white coat hypertensive patients. Patients with white coat hypertension not only show greater blood pressure variability than normal control subjects, but also have a different metabolic and neuroendocrine profile.[90] Some investigators reported that patients with white coat hypertension have moderately increased left atrial dimension[91] and left ventricular mass,[88 91] disturbed diastolic function of the left ventricle[91] or an increased prevalence of silent coronary ischaemia.[92] On the other hand, there is mounting evidence (already discussed) that apart from the few cases misclassified at initial diagnosis, outcome is better correlated with ambulatory blood pressure measurements than with clinic readings[47 68 72–76 78] and that white coat hypertension, therefore, is genuinely a benign condition. In the Syst-Eur trial,[47] to avoid problems with definitions and nomenclature,[93] 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 mm Hg increase in the white coat effect.

HOW TO DEAL WITH WHITE COAT HYPERTENSION

The ambulatory blood pressure monitoring and treatment of hypertension (APTH) trial[87 97] showed that adjustment of antihypertensive treatment based on ambulatory blood pressure monitoring instead of conventional sphygmomanometry may lead to less intensive drug treatment (fig 3) with preservation of blood pressure control, general wellbeing, and inhibition of left ventricular enlargement. Antihypertensive drug treatment may be postponed in 25% of the hypertensive patient population and multiple drug treatment may be avoided in 15%.

The APTH results[87] do not imply that patients with white coat hypertension should be left untreated. However, if no cardiovascular complications are present at diagnosis, treatment could be limited to further follow up and the implementation of cardiovascular hygienic measures—such as regular exercise, reduction of excessive alcohol and sodium intake, and weight reduction.[98] Initial treatment should also account for other cardiovascular risk factors—such as smoking, hypercholesterolaemia, and diabetes mellitus. Whether or not patients with white coat hypertension are at higher risk of developing sustained hypertension remains debated.[99 100] For this reason, once white coat hypertension has been diagnosed, ambulatory blood pressure monitoring should be repeated at annual or biannual intervals.

Management of treatment resistant hypertension

Ambulatory blood pressure monitoring is not only better than conventional sphygmomanometry in selecting patients for antihypertensive drug treatment, but also in assessing the effects of such treatment. Two studies[101 102] showed that changes in ambulatory blood pressure correlated more closely with regression of left ventricular hypertrophy than did the changes in conventional blood pressure. In patients with white coat hypertension, antihypertensive medications lower the clinic but not the ambulatory blood pressure.[94–96] Ambulatory monitoring is therefore an excellent technique to evaluate treatment resistant hypertension (table 3). According to the JNC VI guidelines,[67] other indications for ambulatory monitoring are: hypotensive symptoms under antihypertensive drug treatment, episodic hypertension, and autonomic dysfunction.[103]

The current guidelines do not provide recommendations on the frequency with which ambulatory blood pressure monitoring should be repeated in hypertensive patients on medical treatment. If the initial evaluation shows the absence of a white coat phenomenon, then periodic clinic measurements may be adequate. As in patients with white coat hypertension, in clinical centres where sufficient resources can be allocated, an interval of 1 to 2 years between consecutive recordings seems reasonable, unless there is a special indication for more frequent recordings.[98] The ambulatory blood pressure readings taken when on treatment should be below the thresholds applied for diagnosing sustained hypertension.

Diagnosis of nocturnal hypertension

Ambulatory blood pressure monitoring makes blood pressure measurement during sleep possible (table 3). The hypothesis that non-dipping would be associated with greater cardiovascular risk[104] is not yet generally accepted,[105] although there is accumulating evidence that the night time blood pressure may provide important prognostic information.[47 68] Poor reproducibility of the dipping status[50] and the use of varying definitions for non-dipping[59 68] have contributed to the controversy.

To avoid the use of arbitrary thresholds, the Syst-Eur investigators analysed the night to day blood pressure ratio as a continuous variable.[47]

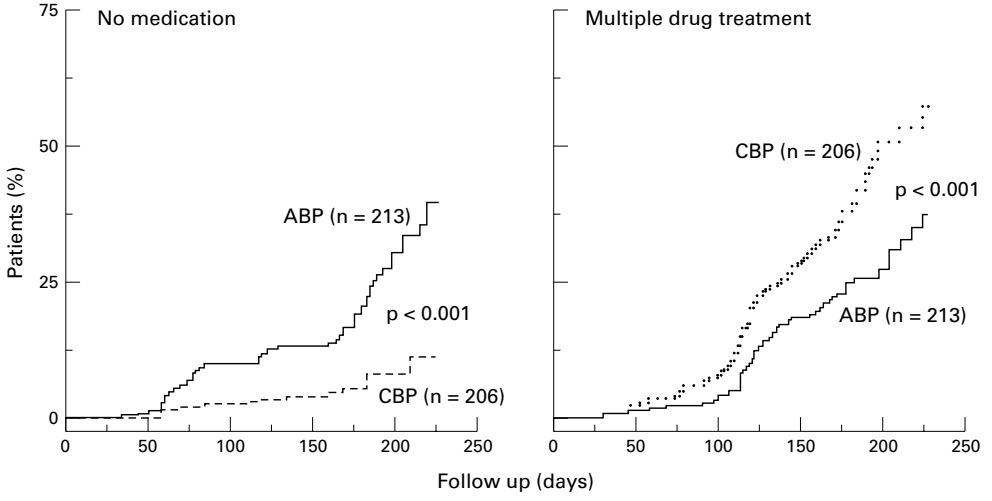

Figure 3 Kaplan-Meier estimates modelling the probability that during follow up patients would permanently stop antihypertensive drug treatment or would proceed to sustained multiple drug treatment. The differences between the patients randomised to conventional (CBP, broken line) or ambulatory (ABP, full line) blood pressure measurement were significant (p<0.001). Reproduced with permission from Staessen et al.[87]

They found that the relative hazard rates associated with a 10 mm Hg increase in the 24 hour systolic blood pressure and with a 10% higher night to day systolic blood pressure ratio were 1.23 (95% CI 1.03 to 1.46; p=0.02) and 1.41 (95% CI 1.03 to 1.94; p=0.03), respectively. Thus, the hypothesis of an inverse association between cardiovascular risk and blood pressure dipping at night was confirmed.[104] Also, the night time blood pressure behaved as a more consistent predictor of major end points than the daytime blood pressure. The variability due to physical activity and psychoemotional stress may weaken the predictive power of the daytime blood pressure, whereas the greater uniformity resulting from sleeping may help to show correlations with the night time blood pressure. The finding that the mean (SD) within subject coefficient of variation was significantly smaller for the night time blood pressure than for the daytime blood pressure (8.7% (3.6%) *v* 10.4% (3.3%); p<0.0001) is in line with this hypothesis.[47] An additional explanation for the close correlation between cardiovascular risk and the night time blood pressure could be that both are linked to a common pathophysiological mechanism—such as a raised sympathetic tone[106] or renal dysfunction—necessitating a higher night time blood pressure to sustain natriuresis.[107]

Patients with secondary hypertension usually have a considerably increased blood pressure, but their diurnal profile is often flattened or even inverted.[108–111] Although not a very sensitive test, when ambulatory monitoring shows severe sustained hypertension, especially in the presence of a non-dipping nocturnal blood pressure, consideration should be given to the possibility of secondary hypertension.

Table 4 Ambulatory blood pressure measuring devices which have been subjected to validation by the BHS[157] and AAMI[163] protocols

Device	*Mode**	*Circumstance*	*AAMI†*	*BHS‡*
Accutracker II	Aus	At rest	P/P	A/C
CH-DRUCK (103)	Aus	At rest	P/P	A/A
Daypress 500	Osc	At rest	P/P	A/B
DIASYS 200	Aus	At rest	P/P	C/C
DIASYS Integra	Aus	At rest	P/P	B/A
	Osc	At rest	P/P	B/B
ES-H531	Aus	At rest	P/P	A/A
	Osc	At rest	P/P	B/B
Medilog ABP	Aus	At rest	P/P	
Meditech ABPM-04	Osc	At rest	P/P	B/B
Nissei DS-240	Osc	At rest	P/P	B/A
OSCILL-IT	Osc	At rest	P/P	C/B
Pressurometer IV	Aus	At rest	F/F	C/D
Profilomat	Aus	At rest	P/P	B/A
		In pregancy	P/P	B/C
Profilomat II	Osc	At rest	F/F	C/B
QuietTrak	Aus	At rest	P/P	B/B
			P/P	A/A
		Different posture		A/A
		During exercise		A/A
		In children		A/A
		In the elderly		A/A
		In pregnancy	F/F	B/B
				A/A
		In pre-eclampsia	F/F	D/D
Save 33 Model 2	Osc	At rest	P/P	B/B
Schiller BR-102	Aus	Passed	P/P	B/B
	Osc	Failed	P/P	B/B
SpaceLabs 90202	Osc	At rest	P/P	B/B
SpaceLabs 90207	Osc	At rest	P/P	B/B
		In children	P/F	C/D
		In elderly people (different posture)	P/P	A/C
		In pregnancy	P/P	A/C
			P/P	B/B
			P/P	B/C
		In pre-eclampsia	F/F	D/D
			P/P	C/C
		During haemodialysis	P/P	C/B
SpaceLabs 90217	Osc	At rest	P/P	A/A
SpaceLabs 90207	Osc	At rest	P/P	B/B
		In children	P/F	C/D
		In elderly people (different posture)	P/P	A/C
		In pregnancy	P/P	A/C
			P/P	B/B
			P/P	B/C
		In pre-eclampsia	F/F	D/D
			P/P	C/C
		During haemodialysis	P/P	C/B
SpaceLabs 90217	Osc	At rest	P/P	A/A
TM-2420/TM-2020	Osc	At rest	F/F	D/D
TM-2420 Model 5	Osc	At rest	P/P	C/C
TM-2420 Model 6	Osc	At rest	P/P	B/B
TM-2420 Model 7	Osc	At rest	P/P	B/B
TM 2421 - Takeda 2421	Aus	In children (different posture)		A/B
	Osc			C/C
Takeda 2430	Osc	At rest	P/P	A/A

*Osc=oscillometric; Aus=auscultatory.
†Criteria for the fulfilment of the AAMI protocol: mean (SD) difference with auscultatory measurements ≤5 (≤8) mm Hg; P/P=passed; F/F=failed; P/F=passed for systolic pressure but failed for diastolic pressure.
‡Grades A–D according to the BHS protocol: A, D=best, worst agreement with mercury standard; according to the BHS protocol devices must achieve at least grade B/B.

Management of hypertension in special groups

OLDER PATIENTS

In the Syst-Eur trial systolic blood pressure was on average 22.0 mm Hg higher (p<0.001) on conventional than on daytime ambulatory measurement.[47 80] The corresponding mean ± 2 SD interval ranged from -8.3 to +52.3 mm Hg.[47 80] These results show that conventional sphygmomanometry, even if repeated at different outpatient visits, may lead to a considerable overestimation of the systolic blood pressure and probably also to excessive treatment of systolic hypertension.

On ambulatory monitoring some older hypertensive patients show striking variability of their diurnal blood pressure with periods of hypotension interspersed with hypertension. This pattern is important to identify so that treatment can be tailored to take account of the fluctuations in blood pressure. In general, older patients are prone to develop hypotension, which may be postural or postprandial[112 113] in nature, may be caused by baroreceptor dysfunction or autonomic failure,[114] or may be the consequence of the greater susceptibility of elderly people to the adverse effects of drugs to lower blood pressure. The identification of symptomatic hypotension constitutes a privileged indication for the clinical use of ambulatory monitoring in elderly people (table 3).[115]

PREGNANCY

Several devices for ambulatory monitoring (table 4) have been specifically validated for use in pregnant women.[116 117] As in the non-pregnant state, the main indication for ambulatory monitoring in pregnancy is the measurement of the white coat effect. Its recognition is important so that pregnant women are not given antihypertensive drugs unnecessarily or excessively. Normal values for ambulatory blood pressure in the pregnant population are available[118 119] and the changes in blood pressure which occur during the trimesters of pregnancy and in the postpartum period have been defined.[119] The evidence that ambulatory blood pressure monitoring may

predict pre-eclamptic toxaemia is not yet conclusive.[120–122] On the other hand, hypertension in pregnancy, as diagnosed with ambulatory monitoring, has been shown to be associated with infants of lower birth weight than in normotensive women.[123]

Self recorded blood pressure

The development of relatively cheap and properly validated devices stimulated the clinical application of self measurement of blood pressure.[124–128] Blood pressure variation through the whole day can only be monitored by ambulatory measurement, but several advantages of that approach can also be accomplished by self measurement.[129 130] The greater number of readings,[127 131] which can be obtained in a practical way, and the absence of the white coat effect[132] contribute to a better diagnostic accuracy compared with conventional sphygmomanometry.[103 133 134] Furthermore, self measurement of blood pressure has been shown to increase compliance to prescribed drugs,[135 136] and to reduce the number of clinic visits required for the diagnosis and treatment of hypertension.[137–139] If automated devices are used,[127] self recorded blood pressure values are also free of observer bias.

The widespread clinical use of self measurement is still limited by the lack of a generally accepted reference frame and operational thresholds for initiating and adjusting antihypertensive treatment. A meta-analysis of the summary statistics of published articles showed that self recorded blood pressure averaged 115/71 mm Hg in normotensive people and 119/74 mm Hg in untreated subjects not selected on the basis of their blood pressure.[13] In an international database of self recorded blood pressures,[140] the 95th percentile in 2401 normotensive people was 136/85 mm Hg for the measurements taken in the morning, 139/86 mm Hg for the measurements obtained in the evening, and 137/85 mm Hg for the self recorded blood pressure regardless of the time of day. This meta-analysis concluded that a self recorded blood pressure above 137 mm Hg systolic or 85 mm Hg diastolic should be considered hypertensive. These thresholds are in close agreement with those for the daytime ambulatory blood pressure (table 2) and with other proposals for self recorded measurements.[13 54 141–143] However, they must be further validated in clinical trials and prospective outcome studies.

Few studies with the goal to validate self recorded blood pressure measurements for cardiovascular risk have been published. In a prospective Japanese population study, the self recorded blood pressure had a stronger predictive power for subsequent mortality than the screening blood pressure.[144] Mancia *et al*[101] found that ambulatory blood pressure measurements correlated better with regression of left ventricular hypertrophy in hypertensive patients than did clinic and self recorded blood pressure measurements. However, in this study[101] the self recorded blood pressure was measured on only one day, once in the morning and once in the evening. Had the self recorded blood pressure been taken over many days, the results might have been different. The treatment of hypertension according to the home or office blood pressure (THOP) trial[145] is currently investigating whether antihypertensive treatment guided by the self measured blood pressure would be more beneficial and cost effective than treatment based on conventional sphygmomanometry.

Choice of devices

Most of the automated blood pressure measuring devices manufactured for use in ambulatory conditions (table 4) or at home use either an auscultatory or an oscillometric method, or a combination of both techniques.[146] The oscillometric, compared with the auscultatory technique, has the advantage of being less costly from an engineering point of view and requires less complex algorithms. Oscillometry can be used in noisy surroundings, such as factories. The oscillometric technique provides readings when an auscultatory gap is present, when the Korotkoff sounds persist until zero pressure—such as in patients with hyperkinetic circulation[147]—or when the sounds are faint—such as in obese subjects. The position of the microphone(s) is a source of error specific to the auscultatory approach.[147] Both methods of measurement, however, are equally affected by dysrhythmias and artifacts of motion.[148] A few devices measure pressure simultaneously by auscultation and oscillometry.[148 149] They provide the means to compare the two techniques in similar conditions.[149] Standard auscultatory readings may be supplemented by oscillometric measurements, whenever the auscultatory cannot be successfully completed, or vice versa.[149]

Most, if not all, manufacturers of monitoring devices refuse to disclose the proprietary algorithms for measuring blood pressure. Moreover, manufacturers tend to modify the devices and algorithms without prior notice.[150–152] Particularly for oscillometric devices, which put empirically derived algorithms into practice, this practice is not acceptable. The guidelines of the British Hypertension Society state that when manufacturers incorporate modifications into externally identical or indistinguishable versions of a model, this should be clearly indicated, and that full details on how the new device differs from earlier versions should be provided.[153] The revision of the British guidelines stressed that it is incumbent upon manufacturers to clearly indicate all modifications in the hardware and software components of automated devices, for instance by changing the device number.[153] Furthermore, modified devices must be subject to a new validation.[153]

There is general consensus among all guidelines[66 67 84 154–157] that only properly validated devices[146] should be used for ambulatory monitoring (table 4) or for the self measurement of blood pressure (Omron HEM-705CP,[158 159] Omron 722C[159] or Omron HEM-713C[160]). The procedures required for the validation have also been thoroughly standardised.[153 157 161–163] Devices can only be considered to have passed validation if the test results have been published as full papers in

peer reviewed journals.[153] Furthermore, when devices are to be used in special patient populations—such as older subjects or pregnant women[116 117 164]—or in special conditions—such as exercise,[148 165] a specific demonstration of accuracy in these defined subgroups and conditions is necessary.[161 164]

Conclusions

The technique of non-invasive ambulatory blood pressure monitoring is now well established as an instrument in clinical research and as a diagnostic tool in clinical practice. Self measurement of blood pressure may become a more cost effective alternative to diagnose white coat hypertension in the near future, but cannot provide information on blood pressure during sleep. These automated techniques minimise misclassification of subjects due to the white coat effect and have over the past two decades found wide acceptance in the management of hypertensive patients,[98] especially in Europe. It is likely that blood pressure measurement in occupational and environmental medicine will follow the same trends as those in clinical medicine.[1]

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