Ambulatory blood pressure in the hypertensive population: patterns and prevalence of hypertensive subforms

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Background A number of clinically identifiable patterns of blood pressure elevation are apparent using ambulatory measurement. Their prevalence and age and sex distribution have not been described. The purpose of this study was to describe the epidemiology of patterns of high blood pressure in a large population.

Design Retrospective database analysis of referral hypertensive population.

Patients Clinic and ambulatory blood pressure measurements were performed in 2092 patients with essential hypertension while they were not taking antihypertensive medication.

Methods The patients were classified into six groups on the basis of their ambulatory blood pressure monitoring profiles: white-coat hypertensives, borderline hypertensives, isolated systolic hypertensives, isolated diastolic hypertensives, combined systolic and diastolic hypertensives and nocturnal hypertensives. The categories were examined for age and sex differences.

Results All patients were categorized into one of the six groups. The majority (56.2%) were systolodiastolic hypertensives, 12.9% were borderline and 10.8% were white-coat hypertensives. Isolated systolic hypertensives comprised 6.2% of the population, isolated diastolic hypertensives 6.9% and nocturnal hypertensives 7.1%. The isolated systolic hypertensives showed the greatest change with age, with a prevalence of < 5% in patients below 40 years of age, rising to almost 20% in the 70

plus age group. White-coat, isolated diastolic and borderline hypertensives showed the opposite change in prevalence, falling from younger to older age groups. Apart from a greater prevalence of white-coat hypertension in females, the patterns were largely similar between sexes.

Conclusions Ambulatory blood pressure monitoring allows the blood pressure pattern to be defined in hypertensive patients. The patterns identified here in a referral hypertensive cohort show changes in prevalence with age, and further study is required to determine the prognostic significance of hypertensive sub-forms. J Hypertens 1998, 16:1735-1743 © Lippincott Williams & Wilkins.

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Introduction

Ambulatory blood pressure monitoring (ABPM) is becoming an indispensable investigation for patients with suspected hypertension [1,2]. The use of ambulatory monitoring in clinical practice has demonstrated that hypertension is not a single pathological entity, denoted by a single blood pressure reading above an arbitrary level, but rather a clinical syndrome manifest by a distinct blood pressure profile. This profile can be categorized as whitecoat hypertension, borderline hypertension, isolated systolic hypertension, isolated diastolic hypertension, systolic and diastolic hypertension, and nocturnal hypertension (Fig. 1). There is a body of evidence that describes separate clinical profiles, actiologies and prognostic data [3–9] in respect of these different patterns of hypertension. The prevalence of the different forms of hypertension as detected by ABPM has not been described previously.

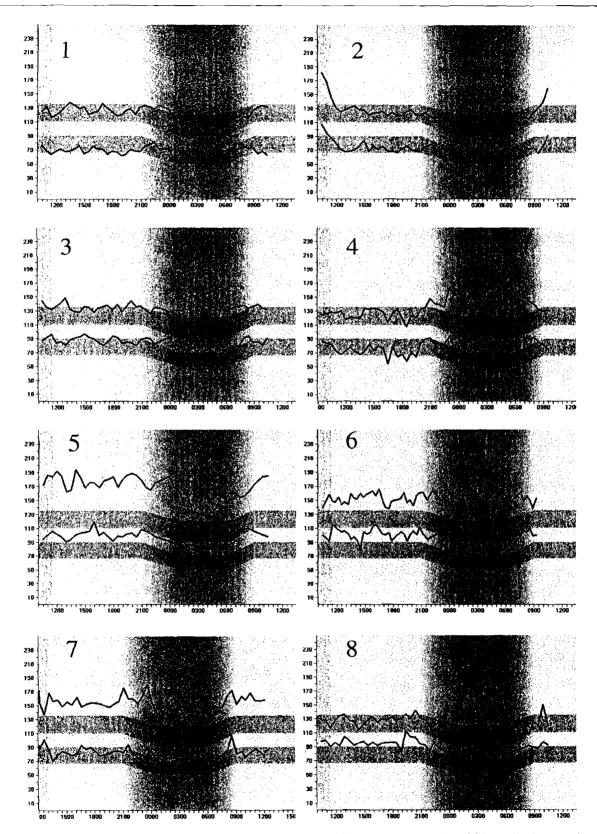
Accordingly, the purpose of this retrospective analysis of patients referred for assessment of hypertension was to identify and categorize the patterns of hypertension revealed by ABPM, and their prevalence in untreated hypertensive patients, and to examine the influence of sex and age on the prevalence patterns as determined by clinic and ambulatory blood pressure.

Patients and methods

Patient population

The population of patients was drawn from the Blood Pressure Unit database, which consisted of all patients

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Examples of ambulatory blood pressure monitoring patterns: (1) normotension; (2) white-coat hypertension; (3) borderline hypertension; (4) nocturnal hypertension; (5) systolic and diastolic hypertension, dippers; (6) systolic and diastolic hypertension, nondippers; (7) isolated systolic hypertension; (8) isolated diastolic hypertension.

referred by their general practitioners or hospital doctors for assessment of hypertension, from 1985 onwards, all of whom underwent ABPM. Hypertension was defined as a referral systolic blood pressure ≥ 140 mmHg and/or a diastolic blood pressure ≥ 90 mmHg [10,11]. Patients included in the population study database for this study were untreated hypertensives. Those patients who were taking antihypertensive medication on attendance at the blood pressure unit were not included in the data collection. Accordingly, all ambulatory blood pressure measurements included in the study were performed on unmedicated patients. Patients with secondary hypertension were not included in the analysis.

Clinical assessment

The patient was assessed by a trained nurse on attendance at the Blood Pressure Unit. Clinic blood pressure was measured according to the recommendations of the British Hypertension Society (BHS) [12]. Pressure was measured after 10 min of quiet rest in the sitting position, and in both arms. Three readings were taken, and the mean of the last two measurements was taken as the clinic blood pressure. Only patients with confirmed hypertensive readings at this stage were included in the study.

Ambulatory blood pressure monitoring

As the database covered a 12 year period, a variety of ABPM devices were used, but 93.8% of the monitors used were either SpaceLabs 90202 or SpaceLabs 90207 (SpaceLabs, Redmond, Washington, USA), which have been validated as fulfilling the BHS and American Association for Medical Instrumentation (AAMI) criteria for accuracy of blood pressure measurement [13,14]. The monitors were applied to the nondominant arm between 0900 h and noon, and the patient was instructed to carry on life as normal between readings but to rest the arm at heart level during readings. The monitors were programmed to measure blood pressure at 30 min intervals day and night. The monitor was removed the next day, and the data were transferred to a personal computer and loaded into a specialized software package (DABL) [15].

The initial, daytime and night-time systolic, diastolic and mean blood pressure were calculated. The initial period was defined as the first hour of monitoring, daytime was defined as the hours between 0900 and 2100 h (excluding the initial period), and night-time as the hours between 0100 and 0600 h. Transition times (2101-0059 h and 0601-0859 h) were not included in the estimates of day and night mean pressures, as these periods represent times during which bed rest is inconsistent and therefore cannot be reliably categorized [16]. Recordings with insufficient data on night-time blood pressure were not included in the analysis. Furthermore, patients on night shift work, or within 4 weeks of completing night shift duty, were not included in the analysis, as shift work may result in an artificially reversed diurnal rhythm [17]. Recordings were not included if there were less than 14 valid readings during the day, or less than seven valid readings during the night; the validity criteria were those identified by the editing software (systolic blood pressure < diastolic blood pressure, diastolic blood pressure > 160 or < 40 mmHg, systolic blood pressure > 260 or < 50 mmHg. Blood pressure values not identified by the editing software were included in the analysis [18].

Definitions and statistical methods

The clinic and ABPM criteria for diagnosis of hypertension and those required for subcategorization into the various blood pressure patterns are presented in Table 1. Systolic and diastolic hypertension was defined as elevation of both systolic and diastolic readings, isolated systolic hypertension as elevation of systolic pressure in the context of normal diastolic readings, isolated diastolic hypertension as elevated diastolic values with a normal systolic mean, nocturnal hypertension as elevated systolic or diastolic nocturnal readings with normal daytime values, white-coat hypertension as elevated clinic pressures with normal diurnal and nocturnal values, and borderline hypertension as the interface between normal and hypertensive (not fitting into other categories). The definition of ABPM norms are based on recommendations taken from a review of population-based normal blood

Table 1 Definitions of hypertension based on clinic and ambulatory blood pressure measurement [17]

Patterns	Definition (mmHg)		
Clinic			
Normotension	< 140 systolic and < 90 diastolic		
Isolated systolic hypertension	≥ 160 systolic and < 95 diastolic		
Isolated diastolic hypertension	< 140 systolic and ≥ 90 diastolic		
Systolic and diastolic hypertension	≥ 140 systolic and ≥ 90 diastolic, or systolic ≥ 140 and < 160 with diastolic < 95, and excluding those defined as ISH		
Ambulatory blood pressure			
Normotension	Diurnal SBP/DBP < 135/< 85, nocturnal < 120/< 70		
White coat hypertension	Clinic SBP ≥ 140 and/or DBP ≥ 90 with normotensive ABPM		
Systolic and diastolic hypertension	Diurnal SBP \geq 140 and DBP \geq 90, or SBP \geq 140 and < 150, with DBP < 90		
Borderline hypertension	Diurnal SBP ≥ 135 and < 140 and/or DBP ≥ 85 and < 90, with normal nocturnal pressures, or		
	Nocturnal SBP ≥ 120 and < 125, and/or DBP ≥ 70 and < 75, with normal diurnal pressures		
solated systolic hypertension	Diurnal SBP ≥ 150 and DBP < 90		
solated diastolic hypertension	Diurnal SBP < 140 and DBP ≥ 90		
Nocturnal hypertension	Diurnal SBP < 140 and DBP < 90, with nocturnal SBP \geq 125 and/or DBP \geq 75		

Results

We identified 9997 ambulatory recordings from different first-time attenders at the blood pressure unit. After excluding treated hypertensives, patients participating in clinical trials and those participating in population prevalence studies, monitors deemed unsuitable for quality control reasons and recordings which were incomplete for 24 h data (Fig. 2), there remained 2092 untreated hypertensive subjects with valid 24 h ABPM tracings, satisfying our quality stipulations, from the referral database. Of these recordings, 91% were from patients attending within the last 5 years. The population as a whole had a mean age of 47.1 ± 13.5 years (range 14-92 years), and was evenly divided between males (49.9%) and females (50.1%). Nonsmokers comprised 63.5% of the population, and a family history of hypertension in a first-degree relative was present in 47.6% of cases.

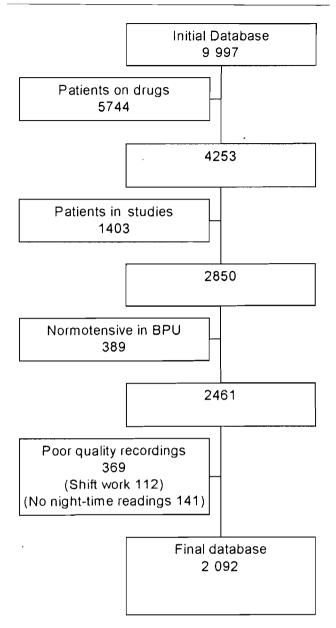
Clinic blood pressure

The mean clinic blood pressure for the group as a whole was 169.8 ± 22.0 mmHg systolic and 102.8 ± 11.5 mmHg diastolic. Applying our definitions (Table 1) to the clinic blood pressure, three categories of hypertension were identified, isolated systolic hypertension, isolated diastolic hypertension, and systolic and diastolic hypertension. The data are outlined in Table 2. Patients with isolated systolic hypertension were older than the other two groups $(51.3 \pm 16.9 \text{ years})$, while patients with isolated diastolic hypertension were much younger $(39.3 \pm 11.8 \text{ years}; P < 0.001)$. Those with systolic and diastolic hypertension $(47.0 \pm 13.0 \text{ years})$ were closer to the patients with isolated systolic hypertension in age.

ABPM patterns and prevalence of hypertension

The patient cohort was divided into categories of blood pressure patterns using the definitions detailed in Table 1. The entire patient population (100%) was categorized on the basis of these six diagnostic groups (Fig. 3). The prevalence of the different hypertensive patterns changed with age, and Figure 4 shows the change in prevalence of hypertensive subforms in each decile of age. The corresponding means and 95% confidence intervals are presented in Table 3. In general, the sexes had broadly similar patterns and prevalence of hypertensive subtypes, and differences were more substantial between older and younger ages, than between males and females (Fig. 3).

Fig. 2

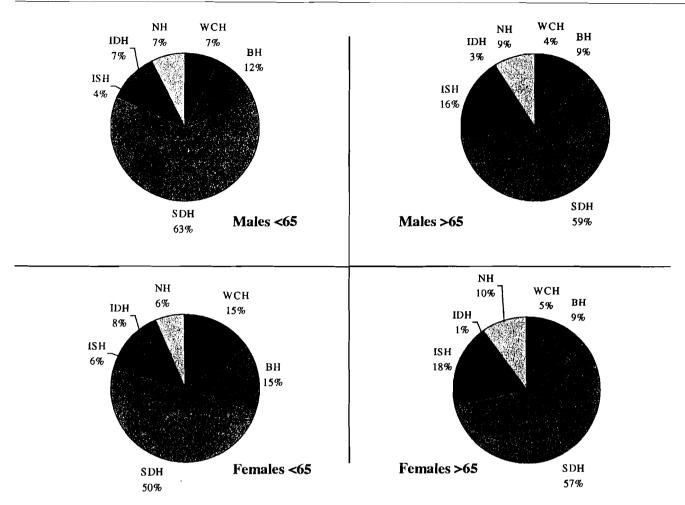


Flow chart of database selection process. BPU, Blood Pressure Unit.

Table 2 Prevalence and clinical characteristics of blood pressure patterns based on clinic blood pressure measurement

	ISH	IDH	SDH
n i	185	75	1832
Prevalence (%)	8.8	3.6	87.6
Sex (male/female)	84/96	48/27	907/919
Age (years)***	51.3 ± 16.9	39.3 ± 11.8	47.0 ± 13.0)

Values are means \pm SD. ISD, isolated systolic hypertension; IDH, isolated diastolic hypertension; SDH, systolic and diastolic hypertension. ***P<0.001, for differences across groups.



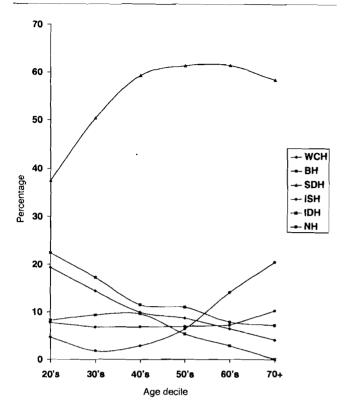
Prevalence of blood pressure subforms in the hypertensive referral population: WCH, white-coat hypertension; BH, borderline hypertension; SDH, combined systolic and diastolic hypertension; ISH, isolated systolic hypertension; IDH, isolated diastolic hypertension; NH, nocturnal hypertension.

The rate of white-coat hypertension in women was more than double that found in men aged under 65 years (15.5 versus 7.4%, $\chi^2 = 29.7$, P < 0.001). Isolated systolic hypertension was also more frequently found in females than in males in this age group (6.2 versus 4.1%, $\chi^2 = 4.3$, P < 0.05). The prevalence of isolated diastolic hypertension (6.8 versus 8.2%, males versus females), whitecoat hypertension (11.9 versus 14.7%) and nocturnal hypertension (8 versus 10%) did not differ significantly between the sexes in patients under 65 years of age. Systolic and diastolic hypertension was significantly more frequent in the male population (62.6 versus 49.1%, $\chi^2 = 34.8, P < 0.001$).

In both sexes, the transition into the more elderly population was marked by a fall in the prevalence of whitecoat hypertension (11.3 versus 4.6%, $\chi^2 = 9.2$, P < 0.01). The prevalence of isolated diastolic hypertension fell in both sexes (males from 6.8 to 2.6%, females from 8.2 to 0.8%; $\chi^2 = 9.08$, P < 0.01). The prevalence of isolated systolic hypertension rose substantially in both groups to approximately one-fifth of all hypertensive patients (males from 4.1 to 15.8%, females from 6.2% to 17.6%; $\chi^2 = 43.2$, P < 0.001). Systolic and diastolic hypertension and nocturnal hypertension did not change significantly in prevalence from the younger to the older age groups, in either sex. In those aged over 65 years, there was no significant sex difference in the prevalence of the different patterns of elevated blood pressure.

The individual age distributions of the hypertensive subforms are shown in Figure 5. Isolated systolic hypertension occurred in a significantly older population (56.0 ± 15.4) than all other types of hypertension. The mean ages for isolated diastolic hypertension (42.6 \pm 10.5), borderline hypertension (43.0 ± 13.5) and white-coat hypertension (41.9 \pm 13.3) were comparable and these conditions were found in significantly younger patients



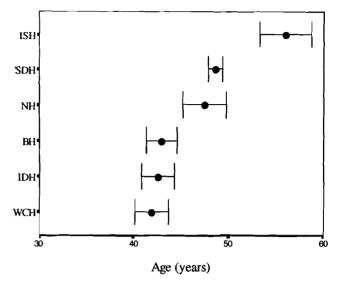


Change in prevalence of hypertensive subforms according to age decile. WCH, white-coat hypertension; BH, borderline hypertension; SDH, combined systolic and diastolic hypertension; ISH, isolated systolic hypertension; IDH, isolated diastolic hypertension; NH, nocturnal hypertension.

than other forms of hypertension. Nocturnal hypertension (47.5 ± 13.8) appeared to occur mainly in an intermediate aged population.

Discussion

Traditional sphygmomanometric measurement of blood pressure has been the mainstay for assessment of blood pressure until relatively recently. The advent of ABPM has allowed not only a more accurate assessment of blood pressure, but it has also been shown to predict end-organ damage more accurately than the traditional method of measurement [21–25], and to improve the quality of management of hypertension.



Age distributions for hypertensive subforms. Markers represent means with error bars showing 95% confidence intervals for the means. WCH, white-coat hypertension; BH, borderline hypertension; SDH, combined systolic and diastolic hypertension; ISH, isolated systolic hypertension; IDH, isolated diastolic hypertension; NH, nocturnal hypertension.

With ABPM, it has become apparent that hypertension is not a simple, general increase in systolic and diastolic blood pressure, but rather, it may be a manifestation of a variety of different patterns. Most widely recognized are the subforms of white coat hypertension and isolated systolic hypertension. The clinical importance of identifying the different patterns of hypertension is twofold: first, an awareness of the patterns may influence treatment, and second, the pattern of ambulatory blood pressure may influence prognosis [26].

The prevalence of these different forms of hypertension has been poorly described. Estimates of prevalence of hypertensive subforms based on sphygmomanometry in the clinic setting suffer from an inability to make blood pressure estimates independently of the white-coat effect [27]. The tendency, therefore, is to overestimate the prevalence of hypertension [28]. Furthermore, ambulatory blood pressure profiles take into account the night-time,

Table 3 Mean proportion (per cent) of patients in each hypertensive category defined using ambulatory blood pressure monitoring according to age decile

Age (years)	n _	WCH	BH	SDH	ISH	IDH	NH _
20-29	192	19.3 ± 5.6	22.4 ± 5.9	37.5 ± 6.8	4.7 ± 3.0	8.3 ± 3.9	7.8 ± 3.8
30-39	383	14.4 ± 3.5	17.2 ± 3.8	50.4 ± 5.0	1.8 ± 1.3	9.4 ± 2.9	6.8 ± 2.5
40-49	554	9.9 ± 2.5	11.5 ± 2.7	59.2 ± 4.1	2.9 ± 1.4	9.6 ± 2.4	6.9 ± 2.1
50-59	553	8.7 ± 2.3	11.0 ± 2.6	61.3 ± 4.1	6.5 ± 2.0	5.4 ± 1.9	7.0 ± 2.1
60-69	277	6.5 ± 2.9	7.9 ± 3.2	61.4 ± 5.8	14.1 ± 4.1	2.9 ± 2.0	7.2 ± 3.0
70+	98	4.1 ± 3.9	7.1 ± 5.0	58.2 ± 9.8	20.4 ± 8.0	0	10.2 ± 6.0

Values are means ± 95% confidence interval; WCH, white-coat hypertension; BH, borderline hypertension; SDH, systolic and diastolic hypertension; ISH, isolated systolic hypertension; IDH, isolated diastolic hypertension; NH, nocturnal hypertension.

sleeping pressure readings, and allow the detection of isolated nocturnal hypertension [29]. In fact the condition of nocturnal hypertension is only amenable to diagnosis using ABPM.

In the present study, we retrospectively identified a large number of patients with hypertension, identified by conventional sphygmomanometry, and determined the prevalence of six subtypes of hypertension, identified by ABPM, in this population. Notably, 18% of hypertensive patients were classified in hypertensive diagnostic categories which are most readily identifiable with the use of ambulatory methods of blood pressure measurement (white-coat hypertension and nocturnal hypertension), emphasizing the importance of ABPM in the management of hypertension.

The prevalence of white-coat hypertension in this study was 10.8%. This is somewhat lower than in other studies. where white-coat hypertension has been found to occur in approximately 20% of hypertensives. However, the diagnosis of this condition is critically dependent on 'normal' ABPM values. Other studies have variably given the prevalence of white-coat hypertension from 12.1% to 53.2% [30-33]. Previous definitions have focused on normal daytime or 24 h pressures as a marker of blood pressure normalcy, when defining white-coat hypertension. We specifically included nocturnal blood pressure values also, and required these also to be normal before making this diagnosis, which may explain the low prevalence found for white-coat hypertension in our population. Indeed, when we defined white-coat hypertension in our population using only daytime pressures on ABPM to define normality, we found the prevalence of whitecoat hypertension to be somewhat higher, at 16.8%. White-coat hypertension was very much more prevalent in females, accounting for approximately 15% of patients with clinic hypertension, compared with approximately 7% in males. The literature is in agreement with this observation [34]. The prevalence of white-coat hypertension fell substantially in the older age group, from 11.3% in those aged under 65 to 5.0% in those aged over 65 years. This is contrary to some previous reports, in which an increase in the prevalence of the white-coat effect [35] and white-coat hypertension has been described with increasing age. Other studies, however, show either an increased incidence of white-coat hypertension in the younger population [36], or no difference in prevalence between young and elderly populations [37]. This, to some extent, undoubtedly reflects differences in definitions of normal blood pressure, but our data from a large sample support the concept of a reduction in the prevalence of white-coat hypertension with age, at least in a hypertensive population.

Isolated systolic hypertension and isolated diastolic hypertension occurred in 6.2% and 6.9% of the hypertensive

population, respectively. Isolated systolic hypertension appears to be a disease of the older population, with patients in this category having a mean age of 56 years. Isolated diastolic hypertension, however, was found in a comparatively young age group (mean 43 years), and did not differ in prevalence between males and females. Isolated systolic hypertension responds well to diuretic therapy, and so identification of a purely systolic hypertensive pattern would allow more specific, guided drug therapy for these patients [38]. Isolated diastolic hypertension is a poorly understood entity, having been described as a prehypertensive state, and as a benign form of blood pressure elevation [39]. With a prevalence of 6.9% in the hypertensive population, and in particular a prevalence of 8.2% in younger females, it is clearly important to identify the true risk and pathological significance of this hypertensive state.

Nocturnal hypertension is a newly recognized condition, in that its identification is dependent on the use of ABPM. It is known that conditions leading to autonomic nervous system derangement, or indeed primary autonomic failure, can lead to reversal of the normal blood pressure fall at night, and the blood pressure profile becomes one of daytime hypotension and nocturnal hypertension [40]. The loss of nocturnal dipping in patients with normal daytime blood pressure results in nocturnal hypertension simply because the normal dipping pattern is absent. In the present study, the nocturnal hypertensive group showed the lowest number and smallest degree of dipping of all five groups. It remains to be seen whether these diurnally normotensive nondippers have a poor outcome with regard to end-organ morbidity and, ultimately, mortality.

To ascribe differing prevalences to these patterns suggests that they can be identified as disease entities in their own right. However, is there any evidence that these conditions have separate aetiologies? The evidence is strongest for isolated systolic hypertension, when the generalized arterial stiffening that occurs with age leads to highvelocity pulse wave reflectance and systolic augmentation of pressure [41]. This fits with the finding that isolated systolic hypertension occurred in a significantly older population than the other forms of hypertension. Whitecoat hypertension has also been identified as occurring in patients with sympathetic hyper-reactivity [42], and although a link with established hypertension has been mooted [43], the evidence is still sparse. Since there is no established association with sustained hypertension, the identification of white-coat hypertension as a separate actiological condition is not unreasonable. Nocturnal hypertension is a new phenomenon; its prevalence may well be understated in the present study, as it required an elevated clinic pressure for patients to be included in the prevalence assessment, and therefore patients with clinic normotension but ambulatory nocturnal hypertension were not included. However, no data are available concerning a separate actiology in respect of this pattern of blood pressure elevation. Isolated diastolic hypertension has been attributed to elevated arteriolar tone in the context of a pliable, elastic central aorta [44]. This would explain its occurrence in our study population in a younger age group.

Borderline hypertension is an obviously artificial category. It was included in the categorization to take account of the uncertainty inherent in classifying patients differently on the basis of a single millimetre of mercury. Also, the normal levels of ambulatory blood pressure are still debated [45], and it was in an effort to account for this 'grey area' in defining an individual as hypertensive or normotensive that the borderline group was included.

Three caveats are important when interpreting the data from this study. The prevalence of any condition is of, course, dependent on the definitions used. This is particularly the case for a condition such as hypertension, in which categorical constraints are placed on continuous variables to provide working concepts such as 'normotension' or 'hypertension'. As there is no definitive cut-off point where pressures above a certain level are harmful and below it are entirely benign, the application of explicit definitions is somewhat arbitrary. In this study, we have used definitions for our hypertensive subforms on the basis of generally accepted criteria for normotension. The values for ABPM normalcy used here are those first recommended by O'Brien and Staessen [19] and similar recommendations were made independently by the American Society of Hypertension [20]. Second, the data used here, although large in volume, were obtained retrospectively, and there is always the spectre of bias when using data that have not been prospectively collected. As the patient population in our database were referrals of hypertensive patients from the community, we may be witnessing a degree of selection bias towards a more moderate to severe hypertensive population. Finally, the value and validity of this division of hypertension into subforms is dependent on the reproducibility of ABPM patterns. The reproducibility of ambulatory measurement as a method of assessing both clinical and trial blood pressure levels has been well documented [46]. Although the reproducibility of circadian variability is disputed, the reproducibility of ABPM patterns, such as those of isolated systolic hypertension or isolated diastolic hypertension, has not yet been satisfactorily established. This study is ongoing.

In reporting these results we are aware that our population is a selected one from a specialized referral clinic, but nonetheless, the patterns of hypertension identified merit consideration and further study in a nonselected group. The prevalence of the various forms of hypertension provides data that are valuable in their own right, as it helps to put into perspective the variety and extent of hypertension in the hypertensive community. The next logical step must be to accurately determine the outcome in terms of morbidity, in the form of end-organ damage, and mortality risk for individual hypertensive subtypes.

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