

# Relationship between blood pressure measured in the clinic and by ambulatory monitoring and left ventricular size as measured by electrocardiogram in elderly patients with isolated systolic hypertension

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**Objective:** To assess the additional diagnostic precision conferred by ambulatory blood pressure monitoring on clinic blood pressure measurement in evaluating the severity of isolated systolic hypertension.

**Methods:** The association between left ventricular size as determined by ECG voltages [R-wave voltages in lead V<sub>5</sub> (RV<sub>5</sub>) and S-wave voltages in lead V<sub>1</sub> (SV<sub>1</sub>)] and blood pressure as assessed by clinic measurements and ambulatory blood pressure monitoring was studied in 97 elderly patients included in the placebo run-in phase of the Syst-Eur trial. The additional diagnostic precision conferred by ambulatory monitoring on clinic blood pressure measurements was assessed by relating the residual ambulatory blood pressure level to the ECG-left ventricular size. The residual ambulatory blood pressure level was calculated by subtracting the predicted ambulatory blood pressure level for each patient (using the linear regression equation relating both techniques for the group) from the observed ambulatory blood pressure.

**Results:** Clinic systolic blood pressure was on average 20 mmHg higher ( $P < 0.001$ ) than daytime ambulatory blood pressure while diastolic blood pressure was similar with both techniques. The sum of SV<sub>1</sub> + RV<sub>5</sub> was significantly related to clinic systolic pressure ( $r = 0.25$ ), and 24-h (systolic,  $r = 0.37$ ; diastolic,  $r = 0.29$ ), daytime (systolic,  $r = 0.30$ ; diastolic,  $r = 0.19$ ) and night-time (systolic,  $r = 0.33$ ; diastolic,  $r = 0.28$ ) ambulatory blood pressure levels. These findings were not affected by adjustment for gender, age and the body mass index. The sum of SV<sub>1</sub> + RV<sub>5</sub> was significantly related to the residual 24-h (systolic,  $r = 0.30$ ; diastolic,  $r = 0.31$ ), daytime systolic ( $r = 0.20$ ) and night-time (systolic,  $r = 0.31$ ; diastolic,  $r = 0.29$ ) ambulatory blood pressure monitoring levels.

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**Conclusion:** Ambulatory blood pressure monitoring adds to the diagnostic precision of clinic blood pressure measurement in assessing the severity of hypertension in this population. The ongoing side project on ambulatory blood pressure monitoring in the Syst-Eur study should establish whether these findings hold true for morbidity and mortality.

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**Keywords:** Clinic blood pressure measurement, ambulatory blood pressure monitoring, ECG-left ventricular size, elderly, isolated systolic hypertension.

## Introduction

The evidence that blood pressure is a powerful predictor of cardiovascular morbidity and mortality is almost exclusively based on clinic measurement [1–3]. Although these data give a good estimate of risk for the population as a whole, the prediction for the individual is relatively weak [4]. While there are relatively few studies to indicate that blood pressure measured by ambulatory monitoring may be a better predictor of cardiovascular mortality and morbidity than clinic pressures alone [5,6], there is ample evidence that ambulatory blood pressure levels are correlated more closely than clinic pressures with several indices of target organ damage [7–16].

The European Working Party on High blood pressure in the Elderly (EWPHE) recently initiated the Syst-Eur study, a randomly allocated trial on the management of isolated systolic hypertension in patients aged over 60 years [17]. The value of 24-h ambulatory blood pressure monitoring in the evaluation and management of hypertension in this group is currently being assessed in a side project to the main trial [18]. A marked discrepancy between blood pressure measured in the clinic and by ambulatory monitoring has been reported in a recent analysis of data from the placebo run-in phase of the Syst-Eur study, where systolic pressure was shown to be 21 mmHg higher by clinic measurements than by daytime ambulatory blood pressure monitoring [19]. This discrepancy raised the important question of how far blood pressure levels obtained with both techniques can be related to target organ damage in this population of elderly hypertensive patients.

In the present work we examined the relationship between the two measurement techniques and target organ damage as indicated by left ventricular size determined by ECG voltages. To assess the additional diagnostic precision conferred by ambulatory blood pressure monitoring on clinic blood pressure measurements in evaluating the severity of hypertension in this population, the association between levels of blood pressure obtained with ambulatory monitoring and ECG-left ventricular size was further analysed after

the contribution made by the clinic measurement to the relationship had been accounted for.

## Patients and methods

### Study protocol

The protocol for the Syst-Eur study has been described in detail elsewhere [17]. In brief, elderly patients with isolated systolic hypertension are admitted to the trial if they (1) are aged 60 years or over at admission to the study; (2) have an average sitting systolic blood pressure of 160–219 mmHg with a diastolic pressure of 94 mmHg or less, measured twice on each of three occasions 1 month apart in the clinic during the run-in phase on placebo; and (3) are willing to cooperate and undergo regular follow-up (informed consent).

### Clinic blood pressure measurement

Clinic blood pressure was measured with a standard mercury sphygmomanometer [20]. Korotkoff phase V was taken as diastolic pressure. During each visit, two measurements were taken 1–2 min apart, with the patient in the sitting position after 3 min of rest.

### Ambulatory blood pressure measurement

The protocol for the side project on 24-h ambulatory blood pressure monitoring in the Syst-Eur study has been described in detail elsewhere [18]. While participation in side projects to the main study is optional, if a centre does agree to participate all patients entered in the main study from that centre must also be entered in side projects, to prevent selection bias.

Non-invasive ambulatory blood pressure was recorded during the placebo run-in phase, at intervals not greater than 30 min, for 24 h. The first ambulatory blood pressure recording of sufficient quality obtained from each patient during the run-in phase was used for analysis.

### ECG technique

Standard 12-lead ECG were obtained during the second visit of the placebo run-in period, following procedures laid down by the Minnesota Code for the standardization of ECG recordings [21]. Only ECG with a calibration signal were included in the analysis. The

R wave voltages in lead  $V_5$  ( $RV_5$ ) and S wave voltages in lead  $V_1$  ( $SV_1$ ) were measured, and the sum of  $SV_1 + RV_5$  was calculated.

#### Statistical analysis

Clinic blood pressure was calculated as the mean of the six measurements taken during the three visits of the run-in phase [17]. Twenty-four-hour ambulatory blood pressure recordings were excluded from analysis when more than 20% of the readings were either missing or technically in error. Each 24-h period was subdivided into four periods, daytime (10 a.m. to 8 p.m.), night-time (midnight to 6 a.m.) and two transition periods. Average ambulatory blood pressure values were calculated for each period. Time-weighted averages of the four intraperiod means were then computed to obtain the mean 24-h blood pressure in each subject.

To calculate the residual ambulatory blood pressure, in order to evaluate the contribution made by the clinic measurement to the relationship between levels of blood pressure obtained by ambulatory monitoring and ECG-left ventricular size, the following method was used. First, a scatter plot was generated by regressing the observed blood pressure levels obtained by ambulatory monitoring on the clinic measurement for each of the patients. From this a regression line and equation for the group as whole was derived (Fig. 1). The patient's clinic blood pressure measurement and the regression equation for the group were then used to calculate a predicted ambulatory blood pressure level for each patient [5]. For instance, the predicted daytime systolic ambulatory blood pressure level for a patient with a clinic blood pressure measurement of 160 mmHg was calculated as follows:

$$18.8I + 0.78S \times 160SBP = 143.6 \text{ mmHg}$$

where I is the intercept, S is the slope and SBP is the systolic blood pressure level by the clinic measurement.

The residual ambulatory blood pressure was then calculated by subtracting, for each patient, the predicted ambulatory blood pressure level from the blood pressure level observed by actual monitoring (Fig. 1) [5,22]. It follows that the residual ambulatory blood pressure is that portion of the observed ambulatory blood pressure level which is independent of the clinic measurement, i.e. it cannot be predicted from the clinic blood pressure and therefore can be used to assess the unique contribution that is made by ambulatory blood pressure levels to ECG-left ventricular size. This residual ambulatory pressure was calculated separately for systolic and diastolic blood pressure levels obtained during the 24-h, daytime and night-time ambulatory measurement periods.

The Statistical Analysis System was used to analyse the data [23]. Statistical methods included Student's t-test and single and multiple linear regression analyses. Data are reported as means  $\pm$  SD.

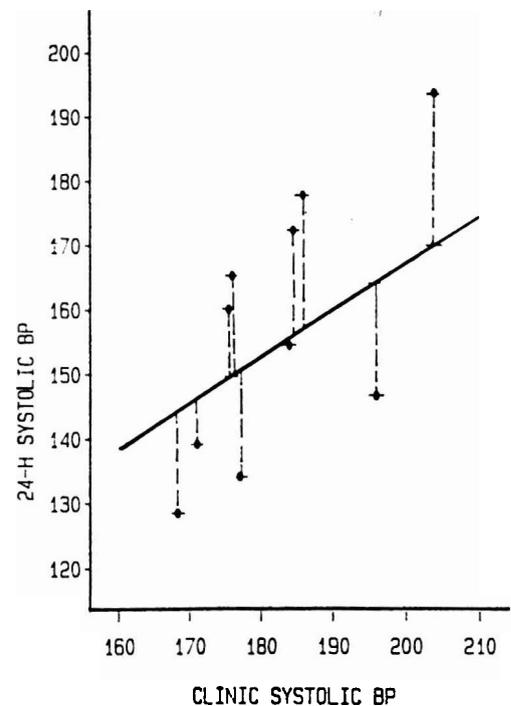


Fig. 1. Regression of observed blood pressure (BP) levels obtained by 24-h ambulatory blood pressure monitoring on those obtained by clinic measurement for each of the 97 patients. The residual 24-h systolic blood pressure is the distance between the observed 24-h systolic pressure and the regression line and is indicated by dashed lines for 10 randomly selected patients.

## Results

### Characteristics of the patients

On 26 October 1991, 753 patients were undergoing randomly allocated treatment in the Syst-Eur trial. Ambulatory blood pressure monitoring data on 102 patients from 16 centres were available for analysis. Four subjects were excluded because their ambulatory blood pressure recording were incomplete and one because the ECG calibration signal was missing, leaving data for 31 males and 66 females ranging in age from 60 to 92 years (median age 71 years). Of these, 65 (47 females) had been treated with antihypertensive agents within the 6 months before entering the placebo run-in period of the study. Treatment status before the study was unknown in one patient. The body mass index was similar in both sexes and averaged  $26.1 \pm 4.2 \text{ kg/m}^2$ .

### Blood pressure and ECG voltages

Levels of blood pressure by both measurement techniques and the ECG voltages are given in Table 1. Systolic blood pressure by clinic measurement was, on average, 20 mmHg higher ( $P < 0.001$ ) than the daytime ambulatory value, 26 mmHg higher ( $P < 0.001$ ) than the 24-h value and 38 mmHg higher ( $P < 0.001$ ) than the night-time blood pressure value by ambulatory monitoring. There was no significant difference

in diastolic blood pressure levels between the clinic measurement and those obtained by ambulatory monitoring. The sum of  $SV_1 + RV_5$  was  $>35$  mm in 15 (15%) of the 97 patients.

**Table 1.** Blood pressure and ECG voltages in 97 patients with isolated systolic hypertension who were followed in the placebo run-in phase of the Syst-Eur study.

Blood pressure (mmHg)	
Clinic systolic	178 ± 12 (160–212)
Clinic diastolic	87 ± 6 (65–95)
24-h systolic	152 ± 15* (120–199)
24-h diastolic	81 ± 9 (59–103)
Daytime systolic	158 ± 16* (132–210)
Daytime diastolic	86 ± 11 (61–112)
Night-time systolic	140 ± 17* (93–179)
Night-time diastolic	71 ± 9 (49–87)
ECG voltages (mm)	
$SV_1$	10.5 ± 4.3 (0–24)
$RV_5$	16.2 ± 6.5 (3–36)
$S_1 + RV_5$	26.7 ± 8.8 (9–58)

Values are expressed as means ± SD (range).  $SV_1$ , S-wave voltage in lead  $V_1$ ;  $RV_5$ , R-wave voltage in lead  $V_5$ . \* $P < 0.001$ , versus clinic systolic measurement.

#### Univariate analysis

$RV_5$  was higher in males than in females ( $18.4 \pm 7.2$  versus  $15.2 \pm 5.5$  mm,  $P < 0.05$ ) while the depth of  $SV_1$  and the sum of  $SV_1 + RV_5$  were similar for both sexes. The ECG voltages were not correlated with age.  $RV_5$  was negatively correlated with the body mass index ( $r = -0.21$ ,  $P = 0.03$ ) whereas  $SV_1$  and  $SV_1 + RV_5$  were not related to the body mass index.  $SV_1 + RV_5$  was significantly and positively related to clinic systolic pressure and 24-h, daytime and night-time systolic and diastolic pressure;  $SV_1$  was related to clinic and night-time systolic pressure and 24-h and daytime systolic and diastolic pressure and  $RV_5$  to 24-h and night-time systolic and diastolic pressure (Table 2).

**Table 2.** Single and partial correlation coefficients relating clinic and ambulatory blood pressures to ECG voltages in 97 patients.

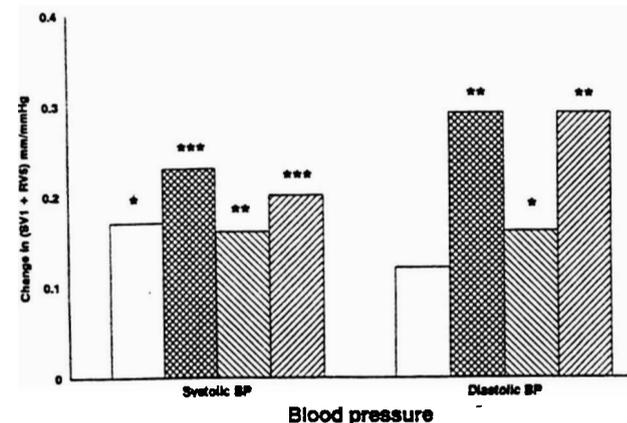
	$SV_1$		$RV_5$		$SV_1 + RV_5$	
	Unadj	Adj	Unadj	Adj	Unadj	Adj
Clinic SBP	0.41***	0.40***	0.06	0.05	0.25*	0.25*
Clinic DBP	0.10	0.09	0.03	0.05	0.07	0.08
24-h SBP	0.44***	0.45***	0.20*	0.22*	0.37***	0.39***
24-h DBP	0.28**	0.30**	0.21*	0.23*	0.29**	0.31**
Daytime SBP	0.42***	0.42***	0.12	0.13	0.30**	0.31**
Daytime DBP	0.27**	0.28**	0.08	0.09	0.19*	0.21*
Night-time SBP	0.32**	0.37***	0.23*	0.26*	0.33**	0.37***
Night-time DBP	0.15	0.18	0.28***	0.29**	0.28**	0.30**

$SV_1$ , S-wave voltage in lead  $V_1$ ;  $RV_5$ , R-wave voltage in lead  $V_5$ ; unadj, unadjusted; adj, adjusted for gender, age and body mass index. \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ .

#### Multiple linear regression analysis

Adjustment for gender, age and the body mass index did not materially alter the relationship between the ECG voltages and the clinic or ambulatory blood pressure levels (Table 2).

The partial regression coefficients for ECG voltages on both the clinic and ambulatory blood pressures are shown in Fig. 2. These regression coefficients indicate that in the case of systolic pressure, a rise in 24-h blood pressure of 10 mmHg was accompanied by a 2.3-mm increase in  $SV_1 + RV_5$ , whereas a similar 10-mmHg rise in the clinic measurement was associated with a 1.7-mm increase. The corresponding results for rises of 5 mmHg in 24-h and clinic diastolic pressure were 1.5 and 0.6 mm, respectively. Although the rise in  $SV_1 + RV_5$  with increasing blood pressure was greater for 24-h and night-time ambulatory pressures than for the clinic pressure, these differences were not significant.



**Fig. 2.** Regression coefficients (adjusted for age, sex and body mass index) relating clinic (□), 24-h (▣), daytime (▤) and night-time (▥) blood pressures (BP) to ECG voltages as assessed by the sum of the S-wave voltage in lead  $V_1$  + the R-wave voltage in lead  $V_5$  ( $SV_1 + RV_5$ ) in 97 patients with isolated systolic hypertension who were followed in the placebo run-in phase of the Syst-Eur study. \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ .

#### Residual ambulatory blood pressure

The  $SV_1 + RV_5$  was significantly and positively related to the residual 24-h and night-time systolic and diastolic blood pressure;  $SV_1$  was related to residual night-time diastolic pressure and 24-h and daytime systolic and diastolic blood pressure, and  $RV_5$  was significantly and positively related to residual 24-h and night-time systolic and diastolic pressure (Table 3). Values for  $r^2$  calculated from Table 3 indicate that residual ambulatory blood pressure levels explained 3–9% of the variability in ECG-left ventricular size.

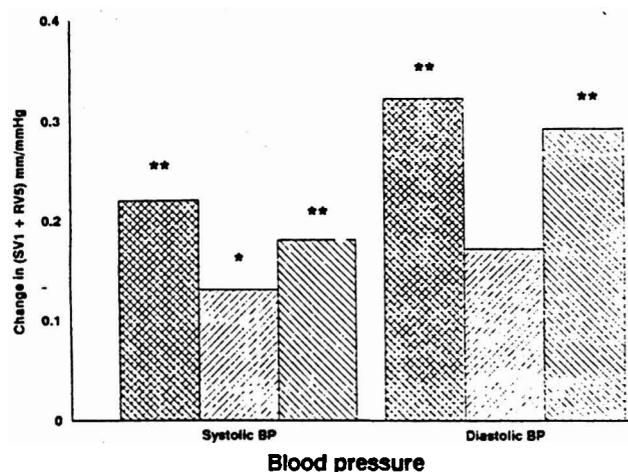
Adjustment for gender, age and the body mass index did not materially alter the relationship between the voltage criteria and the residual ambulatory blood pressure (Table 3). The slopes of the relationships be-

**Table 3.** Single and partial correlation coefficients relating residual ambulatory blood pressures to ECG voltages in 97 patients.

		SV <sub>1</sub>		RV <sub>5</sub>		SV <sub>1</sub> + RV <sub>5</sub>	
		Unadj	Adj	Unadj	Adj	Unadj	Adj
24-h	SBP	0.24*	0.27**	0.21*	0.23*	0.27**	0.30**
	DBP	0.26**	0.28**	0.22*	0.22*	0.29**	0.31**
Daytime	SBP	0.22*	0.22*	0.11	0.12	0.19	0.20*
	DBP	0.26*	0.26**	0.07	0.07	0.18	0.19
Night-time	SBP	0.19	0.25*	0.22*	0.26*	0.26*	0.31**
	DBP	0.13*	0.16	0.28**	0.28**	0.27**	0.29**

SV<sub>1</sub>, S-wave voltage in lead V<sub>1</sub>; RV<sub>5</sub>, R-wave voltage in lead V<sub>5</sub>; SBP, systolic blood pressure; DBP, diastolic blood pressure; unadj., unadjusted; adj., adjusted for gender, age and body mass index. \**P* < 0.05, \*\**P* < 0.01, \*\*\**P* < 0.001.

tween the residual ambulatory pressure and SV<sub>1</sub> + RV<sub>5</sub> are shown in Fig. 3.



**Fig. 3.** Regression coefficients (adjusted for age, sex and body mass index) relating residual 24-h (▨), daytime (▧) and night-time (▩) blood pressures (BP) to ECG voltages as assessed by the sum of the S-wave voltage in lead V<sub>1</sub> + the R-wave voltage in lead V<sub>5</sub> (SV<sub>1</sub> + RV<sub>5</sub>) in 97 patients with isolated systolic hypertension who were followed in the placebo run-in phase of the Syst-Eur study. \**P* < 0.05, \*\**P* < 0.01, \*\*\**P* < 0.001.

## Discussion

In the present study, the clinic measurement of systolic blood pressure was on average 20 mmHg higher than daytime blood pressure levels by ambulatory monitoring (Table 1) as previously reported [16]. Despite this disparity the partial correlation coefficients for clinic systolic pressure ( $r = 0.25$ ,  $P < 0.05$ ) and daytime ambulatory blood pressure ( $r = 0.31$ ,  $P < 0.01$ ) related to SV<sub>1</sub> + RV<sub>5</sub> were similar (Table 2). Levels of systolic and diastolic blood pressure obtained during the 24-h and night-time ambulatory measurement periods were also significantly and positively related to ECG-left ventricular size, especially to SV<sub>1</sub> + RV<sub>5</sub> (Table 2). In addition, the closer relationship between systolic as

opposed to diastolic pressure with left ventricular size as seen in Table 2 is similar to that reported in other studies [16], as is the closer relationship of right than left precordial lead voltages with left ventricular size [24,25].

The additional diagnostic precision conferred by ambulatory blood pressure monitoring on clinic blood pressure measurements in evaluating the severity of hypertension in this elderly population was assessed by examining the association between levels of blood pressure obtained by ambulatory monitoring and ECG-left ventricular size after the contribution made by the clinic measurement to the relationship had been taken into account by calculating the residual ambulatory blood pressure. This was calculated as explained above by subtracting the predicted ambulatory blood pressure level for each patient (using the linear regression equation relating both techniques for the group) from the actual value observed with ambulatory monitoring [5,22]. As the residual ambulatory blood pressure is that portion of the observed ambulatory blood pressure level which is independent of the clinic measurement, it can be used to assess the unique contribution made by the ambulatory blood pressure level to the relationship between ambulatory blood pressure monitoring and ECG-left ventricular size. In the present study, the finding that ECG-left ventricular size was significantly and positively related to residual ambulatory blood pressure (Table 3) confirms the hypothesis that ambulatory blood pressure monitoring adds to the diagnostic precision of clinic blood pressure measurements in evaluating the severity of hypertension in an elderly population.

While most studies have assessed left ventricular mass using echocardiography [9–12,15,16], some have used left ventricular hypertrophy as defined by ECG criteria as part of a score for target organ damage [7,8,13]. In the classic paper by Sokolow *et al.* [7] an aggregated measure of target organ damage based on ECG changes in left ventricular hypertrophy, heart size on chest X-ray and fundal changes was more closely related to daytime pressures than to casual pressures. More recently, Parati *et al.* [13], using a similar composite index of target organ damage, also found a closer correlation between target organ damage and 24-h ambulatory blood pressure than clinic blood pressure. In one study using ECG voltages alone, the orthogonal vector cardiogram system was used to assess left ventricular mass, and a significant correlation ( $r = 0.26$  for systolic and 0.27 for diastolic pressure) was reported between ECG-vectorcardiogram parameters and daytime ambulatory blood pressure values but not clinic blood pressure values ( $r = 0.16$  for systolic and 0.19 for diastolic pressure) [14]. Unfortunately, ambulatory blood pressure monitoring was not used in the EWPHE study, which makes comparisons difficult [26], although the partial correlations between ECG voltages and systolic blood pressure measured in the clinic at random allocation to

groups ( $SV_1$ ,  $r = 0.17$ ,  $P < 0.001$ ;  $SV_1 + RV_5$ ,  $r = 0.15$ ,  $P < 0.001$ ) were similar to those in the present study (Table 2). In contrast to the EWPHE study, where a negative correlation was reported between age and  $SV_1 + RV_5$ , this relationship was not significant in the present study, possibly because of the smaller number of patients ( $n = 97$ ) and the smaller age range (60–92 years).

As treatment with antihypertensive agents may have affected the results, the major calculations were repeated in the 31 patients who were known not to have been treated with antihypertensive agents within the 6 months before entry into the placebo run-in period of the study and also in the 65 patients who were known to have been taking these agents during that period. While the levels of clinic systolic blood pressure tended to be higher in the treated group ( $180 \pm 13/86 \pm 7$  mmHg versus  $175 \pm 10/88 \pm 5$  mmHg in those not previously treated), ambulatory blood pressure levels obtained for the daytime and night-time monitoring periods ( $159 \pm 17/86 \pm 11$  and  $139 \pm 17/70 \pm 9$  versus  $158 \pm 15/88 \pm 10$  and  $141 \pm 15/74 \pm 9$  mmHg, daytime and night-time periods, treated and untreated groups of patients, respectively) and  $SV_1 + RV_5$  ( $26.7 \pm 8.3$  versus  $26.8 \pm 9.8$ ) were similar in both groups. Moreover, partial correlation coefficients for the relationship between levels of systolic blood pressure obtained in the clinic and by ambulatory monitoring during the daytime and night-time periods and  $SV_1 + RV_5$  were similar in both groups ( $r = 0.25$ ,  $P < 0.05$ ;  $r = 0.33$ ,  $P < 0.01$ ;  $r = 0.32$ ,  $P < 0.05$ ; versus  $r = 0.26$ , NS;  $r = 0.22$ , NS;  $r = 0.47$ ,  $P < 0.05$ , respectively in those not previously treated). In addition, partial correlation coefficients relating levels of residual systolic blood pressure for daytime and night-time ambulatory monitoring were also similar in both groups ( $r = 0.22$ , NS;  $r = 0.24$ ,  $P < 0.05$ ; versus  $r = 0.12$ , NS;  $r = 0.43$ ,  $P < 0.05$  in those not previously treated).

Most studies use the correlation coefficient to study the relationship between target organ damage and the level of blood pressure [15,16]. While the correlation coefficient is a measure of the strength of an association between two variables, it is the regression coefficient that enables changes in one variable of interest to be estimated from a given change in another variable. Thus, in the present study, the regression coefficients indicated that a rise in 24-h systolic blood pressure of 10 mmHg was accompanied by a 2.3-mm increase in  $SV_1 + RV_5$ , whereas a similar 10-mmHg rise in the clinic measurement was associated with a 1.7-mm increase. Although the regression slopes tended to be higher for 24-h and night-time blood pressure than for the clinic pressure, these differences were not significant (Fig. 2).

Numerous criteria have been proposed for the estimation of left ventricular size using the 12-lead ECG

[25,27–30]. Improvements in the strength of the correlation between ECG voltages and left ventricular mass have been reported in studies of younger patients using the Cornell criteria [25,31] and the Romhilt–Estes point score [30]. However, in a study of elderly subjects aged 62 years or more the sensitivity of  $SV_1 + RV_5$  or  $RV_6 > 35$  mm as an estimate of left ventricular hypertrophy was 25%, and similar values have been obtained with a Romhilt–Estes point score of  $\geq 5$  (28%) and the Cornell criteria (29%) [32]. Since there seemed to be little gain in using either the Estes ECG scoring system or the Cornell criteria instead of ECG voltages to estimate left ventricular size in older patients, and since the ECG voltages were readily accessible from data already entered on the report forms returned to the Syst-Eur coordinating office, these values were used.

The present study could be criticized because left ventricular size was determined by ECG and not by M-mode echocardiography which is regarded as the method of choice [33]. However, other studies have shown that precordial voltages were significantly and linearly correlated with echo-determined left ventricular mass [34,35]. More importantly, the partial coefficient for clinic systolic blood pressure and  $SV_1 + RV_5$  in the present study was similar to those reported for the relationship between clinic pressure and left ventricular mass assessed by echocardiography in other studies [11,36]. Apart from the fact that echocardiography is not routinely available in all centres taking part in the Syst-Eur study, the use of this technique in large multicentre studies in elderly patients remains debatable as M-mode echocardiography is frequently not possible in obese and older subjects, leading to the exclusion of patients [37] and possible bias in the study sample. Moreover, the sensitivity of ECG detection of left ventricular hypertrophy has been demonstrated to increase with age and may be greater in a population where greater pathological extremes of left ventricular hypertrophy are seen [38], such as the elderly hypertensive group in the present study.

The evidence that isolated systolic hypertension is a powerful predictor of cardiovascular morbidity and mortality in elderly patients is almost exclusively based on clinic measurement [39]. A major objective of the side project on 24-h ambulatory blood pressure monitoring in the Syst-Eur study is to evaluate the extra contribution made by ambulatory blood pressure measurement to the clinic measurement in predicting morbidity and mortality in this age group [18]. While some studies in younger and middle-aged patients have indicated that ambulatory measurement of blood pressure is a better predictor of cardiovascular mortality and morbidity than clinic pressures alone [5,6], it is still not clear whether these findings can be extrapolated to elderly patients with isolated systolic hypertension.

groups ( $SV_1$ ,  $r = 0.17$ ,  $P < 0.001$ ;  $SV_1 + RV_5$ ,  $r = 0.15$ ,  $P < 0.001$ ) were similar to those in the present study (Table 2). In contrast to the EWPHE study, where a negative correlation was reported between age and  $SV_1 + RV_5$ , this relationship was not significant in the present study, possibly because of the smaller number of patients ( $n = 97$ ) and the smaller age range (60–92 years).

As treatment with antihypertensive agents may have affected the results, the major calculations were repeated in the 31 patients who were known not to have been treated with antihypertensive agents within the 6 months before entry into the placebo run-in period of the study and also in the 65 patients who were known to have been taking these agents during that period. While the levels of clinic systolic blood pressure tended to be higher in the treated group ( $180 \pm 13/86 \pm 7$  mmHg versus  $175 \pm 10/88 \pm 5$  mmHg in those not previously treated), ambulatory blood pressure levels obtained for the daytime and night-time monitoring periods ( $159 \pm 17/86 \pm 11$  and  $139 \pm 17/70 \pm 9$  versus  $158 \pm 15/88 \pm 10$  and  $141 \pm 15/74 \pm 9$  mmHg, daytime and night-time periods, treated and untreated groups of patients, respectively) and  $SV_1 + RV_5$  ( $26.7 \pm 8.3$  versus  $26.8 \pm 9.8$ ) were similar in both groups. Moreover, partial correlation coefficients for the relationship between levels of systolic blood pressure obtained in the clinic and by ambulatory monitoring during the daytime and night-time periods and  $SV_1 + RV_5$  were similar in both groups ( $r = 0.25$ ,  $P < 0.05$ ;  $r = 0.33$ ,  $P < 0.01$ ;  $r = 0.32$ ,  $P < 0.05$ ; versus  $r = 0.26$ , NS;  $r = 0.22$ , NS;  $r = 0.47$ ,  $P < 0.05$ , respectively in those not previously treated). In addition, partial correlation coefficients relating levels of residual systolic blood pressure for daytime and night-time ambulatory monitoring were also similar in both groups ( $r = 0.22$ , NS;  $r = 0.24$ ,  $P < 0.05$ ; versus  $r = 0.12$ , NS;  $r = 0.43$ ,  $P < 0.05$  in those not previously treated).

Most studies use the correlation coefficient to study the relationship between target organ damage and the level of blood pressure [15,16]. While the correlation coefficient is a measure of the strength of an association between two variables, it is the regression coefficient that enables changes in one variable of interest to be estimated from a given change in another variable. Thus, in the present study, the regression coefficients indicated that a rise in 24-h systolic blood pressure of 10 mmHg was accompanied by a 2.3-mm increase in  $SV_1 + RV_5$ , whereas a similar 10-mmHg rise in the clinic measurement was associated with a 1.7-mm increase. Although the regression slopes tended to be higher for 24-h and night-time blood pressure than for the clinic pressure, these differences were not significant (Fig. 2).

Numerous criteria have been proposed for the estimation of left ventricular size using the 12-lead ECG

[25,27–30]. Improvements in the strength of the correlation between ECG voltages and left ventricular mass have been reported in studies of younger patients using the Cornell criteria [25,31] and the Romhilt–Estes point score [30]. However, in a study of elderly subjects aged 62 years or more the sensitivity of  $SV_1 + RV_5$  or  $RV_6 > 35$  mm as an estimate of left ventricular hypertrophy was 25%, and similar values have been obtained with a Romhilt–Estes point score of  $\geq 5$  (28%) and the Cornell criteria (29%) [32]. Since there seemed to be little gain in using either the Estes ECG scoring system or the Cornell criteria instead of ECG voltages to estimate left ventricular size in older patients, and since the ECG voltages were readily accessible from data already entered on the report forms returned to the Syst-Eur coordinating office, these values were used.

The present study could be criticized because left ventricular size was determined by ECG and not by M-mode echocardiography which is regarded as the method of choice [33]. However, other studies have shown that precordial voltages were significantly and linearly correlated with echo-determined left ventricular mass [34,35]. More importantly, the partial coefficient for clinic systolic blood pressure and  $SV_1 + RV_5$  in the present study was similar to those reported for the relationship between clinic pressure and left ventricular mass assessed by echocardiography in other studies [11,36]. Apart from the fact that echocardiography is not routinely available in all centres taking part in the Syst-Eur study, the use of this technique in large multicentre studies in elderly patients remains debatable as M-mode echocardiography is frequently not possible in obese and older subjects, leading to the exclusion of patients [37] and possible bias in the study sample. Moreover, the sensitivity of ECG detection of left ventricular hypertrophy has been demonstrated to increase with age and may be greater in a population where greater pathological extremes of left ventricular hypertrophy are seen [38], such as the elderly hypertensive group in the present study.

The evidence that isolated systolic hypertension is a powerful predictor of cardiovascular morbidity and mortality in elderly patients is almost exclusively based on clinic measurement [39]. A major objective of the side project on 24-h ambulatory blood pressure monitoring in the Syst-Eur study is to evaluate the extra contribution made by ambulatory blood pressure measurement to the clinic measurement in predicting morbidity and mortality in this age group [18]. While some studies in younger and middle-aged patients have indicated that ambulatory measurement of blood pressure is a better predictor of cardiovascular mortality and morbidity than clinic pressures alone [5,6], it is still not clear whether these findings can be extrapolated to elderly patients with isolated systolic hypertension.

## Conclusion

The present findings are based on a preliminary analysis of the relationship between blood pressure levels measured in the clinic and by ambulatory monitoring and target organ damage as defined by ECG-left ventricular size in 97 patients who were followed up during the placebo run-in phase of the Syst-Eur study. These findings confirm the hypothesis that ambulatory blood pressure monitoring adds to the diagnostic precision of the clinic blood pressure measurements in evaluating the severity of hypertension in this population. It is expected that the ongoing side project on ambulatory blood pressure monitoring in the Syst-Eur study will establish whether this technique can predict morbidity and mortality due to target organ damage.

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