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ORIGINAL ARTICLE

Ambulatory heart rate and target organ damage in never-treated essential hypertensives

C Cuspidi[1,2], C Valerio[3], S Meani[3], C Sala[3,4], A Esposito[2,3], M Masaidi[3], F Negri[2], V Giudici[2], A Zanchetti[4] and G Mancia[1,4]

[1]*Department of Clinical Medicine and Prevention, University of Milano-Bicocca, Milano, Italy;* [2]*Policlinico di Monza, Monza, Italy;* [3]*Istituto di Medicina Cardiovascolare, Ospedale Maggiore Policlinico Mangiagalli e Regina Elena IRCCS, Milano, Italy and* [4]*Centro Interuniversitario di Fisiologia Clinica e Ipertensione, Università di Milano, Milano, Italy*

Limited evidence is available about the relationship between ambulatory heart rate (HR) and target organ damage (TOD) in uncomplicated hypertension. We sought to investigate the association between ambulatory HR and subclinical cardiac, vascular and renal markers of TOD in never-treated essential hypertensives. A total of 580 subjects with recently diagnosed (⩽1 year) grade 1 and 2 hypertension, categorized by tertiles of HR levels, assessed by two 24-h ambulatory blood pressure monitoring at 1- to 4-week interval, sex and the presence or absence of TOD were considered for this analysis. All subjects also underwent laboratory and ultrasonographic investigations searching for microalbuminuria (MA), left ventricular hypertrophy (LVH) and carotid atherosclerosis (carotid thickening/plaque). In the whole population, as well as in both genders, LVH, carotid atherosclerosis and MA prevalence rates did not significantly increase with 48-h HR tertiles. When patients were categorized according to the presence or absence of TOD (that is, LVH, carotid atherosclerosis or MA) no significant intergroup differences in 48-h HR were found. Furthermore, average 48-h HR was similar in patients without organ involvement as in those with one, two or three TOD signs. Finally, in a multivariate analysis age, 48-h systolic blood pressure and metabolic syndrome assessed by ATP III criteria, but not HR were independently associated with TOD. Our findings showing that 48-h ambulatory HR is not associated with markers of TOD do not support the view that a faster HR may have an additive value in predicting organ damage in the early phases of essential hypertension.

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Introduction

More than 60 years ago, Levy *et al.*[1] for the first time reported an association between a faster heart rate (HR) and cardiovascular morbidity. In the past three decades, a large body of evidence has been showing that a higher HR is an important risk factor for cardiovascular morbidity and mortality as well as for non-cardiovascular death in different clinical settings and in subjects with or without comorbidities.[2] In most longitudinal studies, this association has been found to be independent of traditional risk factors for atherosclerosis or cardiovascular events, such as age and sex.[3]

Correspondence: Professor C Cuspidi, Department of Clinical Medicine and Prevention, University of Milano-Bicocca, Policlinico di Monza, Via Amati 111, Monza, Milano 20052, Italy.
E-mail: cesare.cuspidi@unimib.it
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Several studies have shown that higher HR values are associated with increased blood pressure (BP) levels[4] and that sympathetic hyperactivity is a major determinant of both hypertension and tachycardia;[5] in human hypertension; however, the prognostic significance of HR is based on a few prospective studies showing a positive association between HR and cardiovascular mortality in men but not in women.[6–9]

Furthermore, the relationship between HR and target organ damage (TOD), a powerful predictor of coronary and cerebrovascular events in the hypertensive population, has been investigated by a few studies yielding conflicting results.[10–12]

Due to these elusive data, elevated HR is not listed among the risk factors useful for stratifying total cardiovascular risk and its reduction is not considered a therapeutic target by major hypertension guidelines.[13–16]

The present study was therefore carried out in a large cohort of untreated hypertensives by assessing

ambulatory BP and HR monitoring for two 24-h periods to investigate the association between ambulatory HR and signs of TOD at cardiac, vascular and renal levels.

Methods

Study population
A total of 580 consecutive, never-treated hypertensive subjects referred to our hospital outpatient clinic were included in the study on the basis of their history and on physical and laboratory examination. The inclusion criteria was the presence of grade 1 or 2 hypertension, that is, clinic systolic BP (SBP) values between 140 and 179 mm Hg or diastolic BP (DBP) 90 and 109 mm Hg, diagnosed in the previous 12 months and confirmed during two visits in our clinic. The exclusion criteria were the following: (1) previous history or clinical evidence of congestive heart failure, myocardial infarction, cardiac valve disease, coronary bypass surgery or angioplasty, diabetes mellitus and renal insufficiency; (2) any condition preventing technically adequate ambulatory blood pressure monitoring (ABPM) (for example, atrial fibrillation and other major arrhythmias) and (3) secondary hypertension. After an informed written consent had been obtained, all subjects underwent the following procedures: (1) clinic BP measurements; (2) routine investigations (blood chemistry, urinalysis and 12-lead electrocardiogram at rest); (3) 24-h urine collection for microalbuminuria (MA); (4) two 24-h ABPM at 1- to 4-week interval; (5) an echocardiogram and (6) a carotid ultrasonographic scan. The study protocol was approved by the Ethics Committee of one of the institutions involved.

Blood pressure measurements
Clinic BP was measured at two visits in the outpatient clinic with a mercury sphygmomanometer taking the first and fifth phases of Korotkoff sounds to identify SBP and DBP, respectively. Measurements started after the subjects had been comfortably resting for 5 min in the seated position. Three measurements were taken at 1-min intervals, and the average was used to define clinic BP.

Ambulatory blood pressure monitoring for two periods of 24 h each was carried out in the non-dominant arm using a Spacelabs 90207 device (Spacelabs Inc., Richmond, WA, USA) after validation of reading accuracy against a mercury sphygmomanometer by means of a Y tube. The device was set to obtain BP readings at 15-min intervals during the day (0700–2300) and at 20-min intervals during the night (2300–0700). Subjects were instructed to attend their usual activities and to keep the arm still during measurements; they were also asked to go to bed no later than 2300 and to arise no earlier than 0700; all BP monitorings were performed on a working day (Monday–Friday). Each ABPM data set was first automatically scanned to remove artefactual readings according to pre-selected editing criteria, that is, systolic readings >260 or <70 mm Hg, diastolic readings >150 or <40 mm Hg and pulse pressure readings >150 or <20 mm Hg. Recordings were then analysed to obtain 24-h, daytime and night-time average SBP, DBP and HR; the average of both 24-h recordings was used to define BP and HR values. Nocturnal dipping was defined as a reduction at night in the average SBP and DBP greater than 10% compared to daytime values. Each subject was classified according to the consistency of the dipping and non-dipping status in the first and second ABPM periods as dipper, non-dipper, non-reproducible dipper and non-reproducible non-dipper.

Echocardiography
Technical details have been previously reported.[17] In brief, M-mode, two-dimensional and Doppler echocardiographic examinations were performed with a commercially available instrument (ATL, HDI 3000 or 5000; Bothell, WA, USA). Left ventricular mass (LVM) was estimated from end-diastolic left ventricular internal diameter (LVIDd), interventricular septum and posterior wall thickness (PWT) according to the Devereux's formula[18] and normalized to height$^{2.7}$ to obtain LVM index (LVMI). Relative wall thickness (RWT) was calculated as $(2\times\text{PWT})/\text{LVIDd}$. Patterns of left ventricular geometry were defined according to Ganau *et al*.[19] as follows: LV concentric remodelling was defined by normal LVMI and RWT >0.45, eccentric left ventricular hypertrophy (LVH) by increased LVMI and RWT <0.45 and concentric LVH by increased LVMI and RWT >0.45. LV filling was assessed by mitral flow with standard pulsed Doppler technique and the following parameters were considered: early diastolic peak flow velocity (E), late diastolic peak flow velocity (A) and their ratio (E/A).

Carotid ultrasonography
Technical details have been previously reported.[17] In brief, images of bilateral extra-cranial carotid artery wall (common, bifurcation and internal carotid artery) were obtained in several projections by high-resolution, linear array 7.5–10.0 MHz probes (ATL HDI 3000 or 5000). Plaques were sought in the near and far walls of the entire extra-cranial tree based on the presence of a focal wall thickening. Intima-media thickness (IMT) was measured in the posterior wall of both common carotid arteries at 5, 10, 15, 20 and 25 mm caudally to the bifurcation.[20] To obtain the mean value of common carotid IMT, all five measurements were averaged. Carotid RWT was calculated as $(2\times\text{IMT/Dd})$ where Dd was the value of common carotid internal diameter (intima-intima distance at end diastole).

Microalbuminuria
The concentration of albumin in a 24-h urine sample was measured using a commercially available radioimmunoassay kit (Sclavo SPA; Cinisello Balsamo, Italy). The detection limit of the method was $0.5\,mg\,l^{-1}$. To limit false-positive tests all patients included in the study (1) underwent urinalysis to exclude a concomitant urinary tract infection (2) were advised to avoid heavy physical exercise during the urine collection period.

Definition of target organ damage
Target organ damage was defined by the presence of MA (urinary albumin excretion 30–300 mg per 24 h) or by ultrasonographic evidence of LVH and vascular alterations. LVH was defined as a LVMI equal to or higher than $51\,g\,h^{-2.7}$ in men and $47\,g\,h^{-2.7}$ in women.[21] The presence of at least one carotid atherosclerotic plaque or diffuse IMT was taken as evidence of vascular alterations. A plaque was defined as a focal thickening greater than 1.3 mm in any segment of carotid arteries. Diffuse IMT was diagnosed when the average common carotid wall thickness exceeded 0.8 mm.[14]

Reproducibility of ultrasonographic measurements
As previously reported[22] in our laboratory, intra-observer and inter-observer coefficients of variation for LVMI are 7.4 and 8.6%. The corresponding values for common carotid IMT are 9.2 and 10.1%, respectively.[22]

Statistical analysis
Statistical analysis was performed by the SAS system (version 6.12; SAS Institute Inc., Cary, NC, USA). Values were expressed as means $\pm$ s.d. or percentages. Means were compared by the Student's *t*-test for independent samples. Analysis of categorical data was carried out by χ^2-test or Fischer's exact test when appropriate. The differences within groups were tested by the analysis of variance. The strength of correlation between variables was tested by linear correlation and multiple regression analysis, controlling for several confounders, including age, body mass index (BMI) and BP. The limit of statistical significance was set at $P<0.05$.

Results

Baseline clinical characteristics of the study population divided by gender are shown in Table 1. In men, a trend towards higher values of BMI, serum creatinine, uric acid, LVM, LVMI, carotid IMT and a greater prevalence of ATP III-defined metabolic syndrome (MS) was present. On the contrary, mean age and clinic HR were significantly higher in women.

Tables 2 and 3 show demographic and clinical characteristics of both sexes divided according to tertiles of 48-h HR. In men, ambulatory DBP, BMI, serum triglycerides and prevalence of MS were significantly higher in the upper as compared to the middle and lower HR tertiles. In women, this was the case for ambulatory SBP and DBP, BMI, prevalence of MS and smoking. In both genders, mean age was significant lower in the upper tertile compared to middle and lower ones.

Finally, absolute LVM, but not LVM indexed to height$^{2.7}$, was significantly higher in the lower HR tertile, regardless of gender.

Heart rate and target organ damage
The overall prevalence of LVH, carotid alterations and MA was 27.1, 27.3 and 8.1%, respectively.

No difference in the prevalence of these TOD markers was observed between the middle and

Table 1 Clinical characteristics of the study population

Variables	*Men*	*Women*
n	355	225
Age (years)	44.7 $\pm$ 12.0	47.8 $\pm$ 11.4°
Body mass index ($kg\,m^{-2}$)	26.4 $\pm$ 3.3	23.8 $\pm$ 4.0*
Clinic SBP/DBP (mm Hg)	145.5 $\pm$ 13.3/96.7 $\pm$ 7.9	146.6 $\pm$ 13.7/94.5 $\pm$ 7.5
Clinic heart rate ($beats\,min^{-1}$)	72 $\pm$ 11.0	76 $\pm$ 10.3°
Mean daytime BP (mm Hg)	142.3 $\pm$ 11.3/92.5 $\pm$ 8.1	141.3 $\pm$ 11.2/91.9 $\pm$ 8.8
Smoking (%)	23.3	25.4
MS (ATP III) (%)	33.5	15.3°
Serum uric acid ($mg\,dl^{-1}$)	5.5 $\pm$ 1.2	3.9 $\pm$ 1.0*
Serum creatinine ($mg\,dl^{-1}$)	0.94 $\pm$ 0.15	0.75 $\pm$ 0.14*
LVM (g)	207.4 $\pm$ 40.1	154.2 $\pm$ 34.0*
LVMI ($g\,m^{-2}$)	105.6 $\pm$ 19.0	92.3 $\pm$ 17.9*
LVMI ($g\,h^{-2.7}$)	45.5 $\pm$ 9.4	41.4 $\pm$ 9.0*
E/A ratio	1.2 $\pm$ 0.4	1.2 $\pm$ 0.3
Carotid IMT (mm)	0.67 $\pm$ 0.19	0.63 $\pm$ 0.12
UAE (mg per 24 h)	12.9 $\pm$ 25.8	11.3 $\pm$ 23.8

Abbreviations: BP, blood pressure; DBP, diastolic blood pressure; E/A ratio, peak flow velocity ratio; IMT, intima-media thickness; LVM, left ventricular mass; LVMI, left ventricular mass index; MS, metabolic syndrome; SBP, systolic blood pressure; UAE, urinary albumin excretion.
Data are shown as means $\pm$ s.d. or %.
°$P<0.05$, *$P<0.01$ females vs males.

Table 2 Clinical characteristics of hypertensive men according to 48-h heart rate tertiles

Variables *Heart rate tertile number (beats min^{-1})*	*I (121) 66±5*	*II (119) 75±5*	*III (115) 83±5*
Age (years)	45.3±13.3	45.6±12.1	42.7±9.7°
BMI (kg m^{-2})	26.1±3.3	26.2±3.0	27.1±3.6*
Clinic BP (mm Hg)	146±14/96±9	145±13/96±7	145±12/98±8
Clinic HR (beats min^{-1})	69±9	75±10	81±11
48-h BP (mm Hg)	138±14/86±8	136±11/87±7	138±12/90±8§
Non-dippers (%)	20.1	23.5	24.7
Smokers (%)	20.1	24.3	26.8
MS (ATP III) (%)	25.8	34.4	43.2§
Uric acid (mg dl^{-1})	5.5±1.2	5.4±1.1	5.6±1.2
Creatinine (mg dl^{-1})	0.95±0.16	0.96±0.13	0.93±0.16
Blood glucose (mg dl^{-1})	93.8±10.4	97.9±12.6	96.7±10.5
T cholesterol (mg dl^{-1})	211.5±39.2	216.8±36.5	219.3±48.4
HDL cholesterol (mg dl^{-1})	43.4±12.0	40.2±11.0	40.3±12.4
Triglycerides (mg dl^{-1})	126.8±72.4	144.0±90.5	154.8±101.5°
LVM (g)	216.5±42.9	201.7±37.7	201.1±36.5§
LVMI (g h$^{-2.7}$)	47.3±10.1	44.6±9.1	44.8±8.5
IVSTd (mm)	10.4±1.1	10.2±0.9	10.3±1.0
PWTd (mm)	9.6±0.9	9.4±0.9	9.4±0.7
Left atrial size (mm)	37.4±4.0	36.9±4.1	36.7±4.3§
E/A ratio	1.2±0.4	1.2±0.4	1.2±0.3
Carotid IMT (mm)	0.69±0.19	0.66±0.14	0.66±0.15
UAE (mg per 24 h)	11.9±18.5	12.3±25.1	12.9±24.5

Abbreviations: BP, blood pressure; BMI, body mass index; E/A ratio, peak flow velocity ratio; HDL, high-density lipoprotein; HR, heart rate; IMT, intima-media thickness; IVSTd, interventricular septum thickness diastole; LVM, left ventricular mass; LVMI, left ventricular mass index; MS, metabolic syndrome; PWTd, posterior wall thickness diastole; T cholesterol, total cholesterol; UAE, urinary albumin excretion.
°$P<0.05$, *$P<0.01$, III vs II and I; §$P<0.05$ III vs I.

Table 3 Clinical characteristics of hypertensive women according to 48-h heart rate tertiles

Variables *Heart rate tertile number (beats min^{-1})*	*I (70) 68±3*	*II (72) 76±3*	*III (83) 85±6*
Age (years)	52.5±12.5	50.5±9.7	43.3±10.3*
BMI (kg m^{-2})	23.4±2.5	23.5±3.5	24.2±4.3
Clinic BP (mm Hg)	150±14/94±8	144±12/93±7	146±14/96±8
Clinic HR (beats min^{-1})	71±9	73±8	81±10
48-h BP (mm Hg)	133±10/83±7	135±10/85±8	137±11/90±9§
Non-dippers (%)	28.5	11.0	31.0
Smokers (%)	19.0	19.7	33.0§
MS (ATP III) (%)	11.5	10.9	20.0§
Uric acid (mg dl^{-1})	3.9±1.0	3.9±0.8	3.9±1.1
Blood glucose (mg dl^{-1})	92.1±13.9	90.1±10.7	88.5±9.9
Creatinine (mg dl^{-1})	0.71±0.14	0.76±0.14	0.76±0.14
T cholesterol (mg dl^{-1})	216.4±32.6	221.0±37.6	216.5±42.5
HDL cholesterol (mg dl^{-1})	58.5±19.5	53.3±15.3	54.9±16.2
Triglycerides (mg dl^{-1})	100.3±39.1	94.2±48.5	107.3±61.1
LVM (g)	164.9±33.9	151.7±31.6	150.4±34.8°
LVMI (g h$^{-2.7}$)	44.1±8.5	41.9±9.0	40.3±9.4
IVSTd (mm)	9.6±1.1	9.1±0.9	9.2±1.0
PWTd (mm)	8.9±0.8	8.4±0.7	8.5±0.8
Left atrial size (mm)	34.8±3.7	32.9±3.9	32.5±3.7°
E/A ratio	1.1±0.4	1.2±0.3	1.2±0.3
Carotid IMT (mm)	0.66±0.12	0.63±0.11	0.62±0.13
UAE (mg per 24 h)	10.3±10.8	11.2±13.8	11.4±32.4

Abbreviations: BP, blood pressure; BMI, body mass index; E/A ratio, peak flow velocity ratio; HDL, high-density lipoprotein; HR, heart rate; IMT, intima-media thickness; IVSTd, interventricular septum thickness diastole; LVM, left ventricular mass; LVMI, left ventricular mass index; MS, metabolic syndrome; PWTd, posterior wall thickness diastole; T cholesterol, total cholesterol; UAE, urinary albumin excretion.
°$P<0.05$ III vs I; *$P<0.05$ III vs II and I; §$P<0.05$ III vs II and I.

upper HR tertiles in the whole study population as well as in both genders.

A greater prevalence of carotid atherosclerosis (carotid thickening/plaque) was found in women in the lower HR tertile compared to those in the upper tertile. This was also the case for LVH in men (Figure 1). These differences, however, did not remain significant after controlling for age.

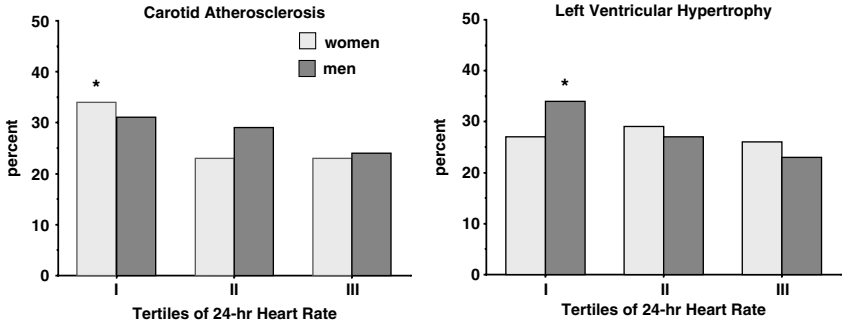

Figure 1 Prevalence rates of LVH and carotid atherosclerosis in female (grey bars) and male (black bars) essential hypertensives across 48-h HR tertiles. $^*P<0.01$.

Table 4 Clinic and 48-h heart rate in hypertensive females and males with and without target organ damage

Variables	*LVH+*	*LVH−*	*CA+*	*CA−*	*MA+*	*MA−*
Females (*n*)	60	165	61	164	29	196
Clinic HR (beats min^{-1})	77±7	77±9	75±8	78±9	78±7	77±9
48-h HR (beats min^{-1})	77±8	78±8	77±8	78±8	77±7	78±8
Males (*n*)	97	258	98	257	48	307
Clinic HR (beats min^{-1})	73±9	76±10	74±9	74±9	74±10	75±10
48-h HR (beats min^{-1})	72±9	75±8	74±9	76±9	74±8	74±9

Abbreviations: CA, carotid atherosclerosis; HR, heart rate; LVH, left ventricular hypertrophy; MA, microalbuminuria.

When patients were categorized according to the absence or presence of any sign of TOD (that is, with or without LVH, carotid atherosclerosis or MA) no significant intergroup differences in both clinic and 48-h HR levels were found (Table 4).

In a further analysis, subjects were classified according to the number of organs involved (that is, 0, 1, 2 or 3 organs). Average 48-h HR was similar in patients without organ involvement (76±8 beats min^{-1}) as in those with a single (75±8 beats min^{-1}), two (74±9 beats min^{-1}) or three signs of TOD (75±8 beats min^{-1}).

In the whole study population 48-h HR as a continuous variable showed positive correlations with clinic DBP ($r=0.13$, $P<0.001$), 48-h DBP ($r=0.24$, $P<0.0001$), daytime DBP ($r=0.24$, $P<0.0001$) and night-time DBP ($r=0.21$, $P<0.0001$). A significant inverse relationship was found between 48-h HR and age ($r=0.12$, $P=0.002$), body surface area ($r=0.11$, $P=0.006$), serum creatinine ($r=0.13$, $P=0.007$), LVM ($r=0.27$, $P<0.0001$) and LVM/height$^{2.7}$ ($r=0.25$, $P<0.0001$).

Logistic regression models were constructed to evaluate the independent contributions of different factors on LVH, carotid atherosclerosis and MA: these models included age, gender, 48-h HR, clinic SBP/DBP, ambulatory SBP/DBP, overweight and MS. Among these variables, only age (⩾50 years), 48-h SBP (⩾140 mm Hg) and MS were independently associated with LVH, carotid atherosclerosis and MA. No such association was found for 48-h HR; in fact, for each s.d. increase in 48-h HR odd ratios for cardiac, vascular and renal TOD were 0.78 (95% confidence interval (CI) 0.45–1.71, $P=$ not significant), 0.84 (95% CI 0.56–1.34, $P=$ not significant) and 0.71 (95% CI 0.48–1.61, $P=$ not significant), respectively.

Discussion

The main finding of this study in 580 untreated hypertensive subjects is the lack of any independent association between HR, derived from 48-h ambulatory BP monitoring, and markers of cardiac and extracardiac TOD, such as LVH, carotid atherosclerosis and MA. This investigation for the first time analysed the relationship between HR based on two ABPMs, performed at 1- to 4-week interval and organ involvement at cardiovascular and renal level in a representative sample of uncomplicated subjects of both genders with mild-to-moderate essential hypertension.

Several aspects of our results deserve to be commented. In univariate analyses no positive association between HR and LVM, carotid IMT or urinary albumin excretion (UAE) was found. On the contrary, an inverse relation between 48-h HR and LVM, carotid IMT was observed. This finding is in accordance with Armario *et al.*[23] who found an inverse relationship between resting HR recorded during an echocardiographic examination and LVM in 142 hypertensives and with Zakapoulos *et al.*[12] who observed a negative relation between mean 24-h HR and cardiac mass in 250 hypertensives. At difference from Zakapoulos *et al.*, however, an

independent association between HR and LVM or carotid atherosclerosis was not confirmed by the multivariate analysis performed in our study, thus suggesting that confounders such as age, sex and BMI were probably responsible for those previous results.

Other findings of our study do not support an association between TOD and elevated HR in the early phases of uncomplicated hypertension. First, no significant increases in the prevalence of TOD was found across the HR tertiles in both genders when preclinical organ involvement was defined by the presence or absence of LVH, carotid wall thickening/plaque and MA. On the contrary, men and women in the lower 48-h HR tertile showed a greater prevalence of LVH and carotid atherosclerosis than their counterparts in the middle and upper tertiles, although the difference was no more statistically significant when adjusted for several confounders. Second, patients with a single TOD had a similar HR as those without organ involvement or with two or three signs of TOD.

It is worth noting that the involvement of one or two target organs was rather frequent in our series; the prevalence rates, indeed, of LVH, carotid alterations (that is, carotid plaques and/or carotid thickening) and MA were 28, 27 and 8, respectively. Moreover, left ventricular concentric remodelling was present in an additional 10% of patients and the prevalence of MA defined according to the less conservative threshold (that is, 20–300 mg per 24 h) recommended by International Society of Hypertension/World Health Organization guidelines[16] was approximately 14% (data not shown). Thus, only 45% of our subjects were apparently free from any cardiac and extracardiac involvement: it is unlikely, therefore, that we failed to observe a correlation between HR and subclinical cardiovascular alterations due to a low prevalence of TOD in the whole population.

The following points of our results may deserve a further discussion.

Several studies have reported that faster resting HRs are associated with higher BP levels. The association between clinic HR and BP has been observed in large population-based studies across a wide range of age and BP values, with correlation coefficients generally higher for SBP than for DBP.[3,24] In our study, however, a positive correlation was found between 48-h HR and 48-h daytime and night-time DBPs, but not SBP. This finding may be explained by demographic and clinical characteristics of our sample, prevalently composed by young subjects with grade 1 hypertension. In this setting diastolic hypertension represents the prevalent BP phenotype. The lack of a positive association between HR and a powerful predictor of TOD, such as systolic load recorded throughout 48-h in our model, may in part explain why a faster HR does not play a role in the hypertensive damage. The influence of several variables such as the autonomic nervous system, age and gender in our present results should be also considered. An increase in HR may be related to the sympathetic hyperactivity frequently observed in young subjects with borderline or grade 1 hypertension, in women or in untrained sedentary subjects. Although differences in the degree of physical activity across the HR tertiles cannot be excluded, it should be pointed out that subjects performing intense regular physical activity were excluded from the study. As for the influence of age and gender, in the whole population an elevated HR was associated with younger age and female sex, two conditions characterized by a low cardiovascular risk. It is unlikely that the potential association of HR and TOD was underestimated in our analysis that was based on HR derived from 48-h ambulatory BP monitoring—a large body of evidence, indeed, indicate that ambulatory HR is more reproducible than clinic HR,[25] which is largely influenced by a number of environmental stimuli, including the alerting reaction induced by the medical visit.

Among the limitations of our study, at first, it should be pointed out that our findings are based on a cross-sectional design and further studies are needed to investigate the role of ambulatory HR in predicting cardiac and extracardiac organ involvement during long-term follow-up. Second, our data refer to a selected sample of Caucasian subjects with uncomplicated grade 1–2 hypertension and should not be generalized to the hypertensives with different clinical, demographic and ethnical characteristics.

In conclusion, the present study failed to observe an independent association between ambulatory HR and several markers of TOD, such as LVH, carotid atherosclerosis and MA in a hypertensive population. Thus, our findings do not support the view that a faster ambulatory HR may have an additive value over well-established factors (such as age, BP and metabolic variables) in predicting TOD in the early phases of essential hypertension.

What is known about this topic

- An association between a faster heart rate and cardiovascular morbidity and mortality has been reported in a number of prospective studies[2,3]
- The relationship between heart rate and target organ damage has been investigated by a few cross-sectional studies yielding conflicting results[10–12]

What this study adds

- Our analysis, based for the first time on heart rate derived from 48-h ambulatory BP monitoring, clearly shows a lack of association between heart rate and different markers of target organ damage, such as left ventricular hypertrophy and microalbuminuria
- Thus, our findings do not support the view that a faster ambulatory heart rate may have an additive value to other well-established factors (such as age, BP and metabolic variables) in predicting target organ damage in the early phases of essential hypertension

Conflict of interest
None.

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