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Clinic blood pressure, ambulatory blood pressure and cardiac structural alterations in nonagenarians and in centenarians

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Abstract

scant information is available on the alterations in cardiac structure and function characterizing very elderly people as well as on their relationships to clinic and ambulatory blood pressure (BP) values. In 106 subjects aged 95.3 ± 3.7 years (mean ± standard deviation, 89 nonagenarians and 17 centenarians) in good clinical conditions and living in the municipal house in Milan, we measured, along with standard clinical and laboratory variables, clinic BP, 24-h ambulatory BP and echocardiographic parameters. Forty-five of the recruited subjects were normotensive individuals, whereas 61 were treated hypertensive patients. Subjects with an age greater than 90 years showed clinic systolic (SBP) and diastolic BP (DBP) both within the normal range, with values that for clinic SBP were slightly lower than the corresponding 24-h SBP (120.8 ± 15.9 vs 128.0 ± 16.3 mmHg) and for DBP slightly higher (69.7 ± 8.8 vs 64.9 ± 8.0 mmHg). Daytime average mean BP was slightly lower than night-time average mean BP, indicating the attenuation of the BP reduction during night-time. Left ventricular mass index (LVMI) was increased and significantly related to both 24-h and clinic BP values ($r = 0.24$, $p < 0.04$ and $r = 0.20$, $p < 0.05$). Thus in nonagenarians and centenarians, abnormalities in left ventricular pattern are of frequent detection and may be related both to the ageing process and to BP load.

Key Words: *aging, ambulatory blood pressure, centenarians, clinic blood pressure, left ventricular mass, very elderly*

Introduction

Several studies have described the haemodynamic and metabolic characteristics of subjects belonging to the more advanced age strata (1–6). However, data on individuals above 90 years of age are still limited, particularly with regard to the 24-h blood pressure (BP) profile and its relationship to clinic BP and cardiac structure and function.

In the present study, we report the results obtained by examining subjects aged more than 90 years from the population ($n = 1000$) living in an elderly house (ASP IMMeS Pio Albergo Trivulzio, University of Milan) belonging to the municipality of Milan (Italy). In addition to the subjects' clinical history, the examination included laboratory and metabolic variables, an electrocardiogram, an echocardiogram and clinic and ambulatory BP measurements, allowing an extensive description of their characteristics as well as relationships.

Methods

All subjects living in the elderly house between November 2009 and May 2010 were studied, provided that their age was above 90 years, they displayed a sufficient degree of personal and motor autonomy, including performance of the usual daily activities of elderly people, and there was no advanced alteration of the cognitive function that could prevent proper collection of the data. The study protocol was approved by the institutional Ethics Committee of the University of Milan. All patients gave written consent to the study after being informed of its nature and purposes. Along with routine laboratory

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examinations (which were all in the normal age range values) data collection specific for the present study consisted of (i) subjects' clinical history; (ii) physical examination, including body weight and body mass index, calculated as the ratio between weight in kilograms and the square of height in meters; (iii) fasting plasma glucose, lipids and creatinine from a venous blood sample, with calculation of the estimated glomerular filtration rate via Cockroft & Gault formula $[(140 - \text{age}) \times \text{weight}]/\text{creatinine} \times 72$ ($\times 0.85$ if female) (7); (iv) clinic and 24-h ambulatory BP; (v) an electrocardiogram; (vi) an echocardiogram; and (vii) cognitive function as assessed by the Mini-Mental State Examination (8). Clinic BP was measured three times with the subject having been in a sitting position for 5 min, using a mercury sphygmomanometer and taking the first and fifth Korotkoff sounds to identify systolic (SBP) and diastolic (DBP) values, respectively. Heart rate was measured by the palpatory method over 60 s after each BP measurement. In each subject, the three clinic BP or heart rate measurements were averaged. This was also done for pulse pressure (difference between SBP and DBP) as well as for mean BP (DBP + 1/3 of pulse pressure). Ambulatory BP was measured by a validated semiautomatic device (Spacelabs 90207) (9) over the 24-h period, setting the equipment to provide one value every 15 min during the day (07:00 to 23:00 h) and one value every 20 min during the night (23:00 pm to 07:00 h). In each subject, the 24-h, the daytime and the night-time SBP and DBP were analysed and expressed together with the corresponding standard deviations. This was also done for ambulatory pulse pressure and heart rate values. The procedure was well tolerated and no patient reported interference with daily activities or nighttime sleep.

M-mode, two-dimensional and Doppler echocardiographic examinations were performed with the patient lying on the left size, using a commercially available instrument Sonoline G50 (Siemens). To obtain the best quality images, recordings were obtained at the end of expiration, employing the parasternal and apical windows. All measurements were collected by the same skilled operator and read by an independent observer (intraobserver coefficients of variation 0.6% for left ventricular end-diastolic diameter, 3.3% for interventricular wall thickness and 3.4% for left ventricular posterior wall thickness). The echocardiographically derived variables that were considered in the present study were left ventricular end-diastolic diameter, end-diastolic interventricular septum and posterior wall thickness, left ventricular ejection fraction (modified Simpson formula), transmitral telediastolic (E) and protodiastolic (A) flow velocity peak, as well as their ratio and deceleration time. The last two variables were regarded as markers of diastolic function. Left ventricular mass was calculated by the American Society of Echocardiography formula $(0.83 \times ((D + T)^3 - D^3) + 0.6)$ (10) and left ventricular mass index (LVMI) was obtained by dividing left ventricular mass for body surface area or height (10). Left ventricular hypertrophy was defined as a LVMI ≥ 125 g/m^2 (≥ 51 g/h$^{2.7}$) in men and ≥ 110 g/m^2 (≥ 47 g/h$^{2.7}$) in women. Eccentric and concentric types of left ventricular hypertrophy were assessed based on standard criteria (11). To obtain data on left ventricular remodelling, calculation was also made of the left ventricular thickness/radius (h/r) ratio, which was considered normal if ≤ 0.42.

Data analysis

In each subject, averages were obtained for clinic and ambulatory BP values, which were first edited from artifacts (9). Valid ambulatory SBP and DBP readings were 89.1% and 88.9%, respectively, of the planned 88 readings. The statistical analysis was performed by the SAS system (version 6.12, SAS Institute Inc., Cary, North Carolina, USA). Values were expressed as means ± standard deviation or as per cent data of the group as a whole or of subgroups. Continuous variables were compared by analysis of variance (ANOVA), using Student's *t*-test for dual comparisons. When appropriate, adjustment was made for age, gender, SBP, DBP and other potential confounders using analysis of covariance. Pearson correlation coefficients were used to determine the relationship between different variables. A multivariate analysis was also performed with office, 24-h SBP and DBP, age, gender, blood glucose, plasma creatinine as the independent variables and LVMI as the dependent variable to determine the variables independently predictive of the development of LVMI alterations. A p-value < 0.05 was taken as the minimal level of statistical significance.

Results

General characteristics

The general demographic and clinical characteristics of the 106 subjects studied are shown in Table I. Average age was 95.3 ± 3.7 years with a high prevalence of females (85.4%). Body mass index and lipid profile were well within the normal range and so were serum glucose and creatinine although the estimated glomerular filtration rate resulted into a lower value. About one quarter reported a history of myocardial infarction or heart failure, which were more common than a history of stroke. A history of hypertension was common, being detectable in 57.5% of the patients; 95% of the hypertensive patients were treated, 47% of which with more than one drug. About two-thirds of the population studied did not show any evidence of cognitive

Table I. Demographic and clinical characteristics of the whole population studied and of the two subgroups of normotensive (NT) and hypertensive (HT) subjects.

	All subjects ($n = 106$)	NT ($n = 45$)	HT ($n = 61$)
Age (years)	95.3 ± 3.7	95.2 ± 3.4	95.4 ± 4.0
Female prevalence (%)	85.7	84.4	86.6
Body mass index (kg/m^2)	22.2 ± 4.1	20.5 ± 3.1	23.3 ± 4.3**
Total cholesterol (mg/dl)	171.5 ± 28	165.3 ± 26	176.2 ± 29
Triglycerides (mg/dl)	108.0 ± 34	95.1 ± 28	117.5 ± 41
HDL-cholesterol (mg/dl)	44.2 ± 11	41.1 ± 12	45.9 ± 11
Blood glucose (mg/dl)	88.6 ± 18	86.1 ± 22	90.5 ± 16
Serum creatinine (mg/dl)	1.1 ± 0.4	1.0 ± 0.4	1.1 ± 0.4
Glomerular filtration rate (ml/min)	32.4 ± 9	30.4 ± 8	33.9 ± 12
History of MI (%)	13.3	11.4	14.2
History of CHF (%)	12.4	14.9	9.3
History of stroke (%)	10.3	9.1	11.1
History of hypertension (%)	57.5	0	100**

Data are shown as means ± standard deviations. Asterisks (**$p < 0.01$) refer to the statistical significance between NT and HT subjects. HDL, high-density lipoprotein; MI, myocardial infarction; CHF, congestive heart failure.

impairment, whereas in the remaining third a cognitive impairment of mild degree, however, without significant disability and impairment of daily life usual activities, was found.

Figure 1 shows average BP values. Clinic SBP and DBP were both well within the normal range with values that for SBP (but not for DBP) were slightly less than the corresponding 24-h values. Daytime DBP values were slightly lower than the corresponding night-time DBPs, but this was not the case for SBP. Clinic heart rate was normal and similar to daytime heart rate. Night-time heart rate showed a small but significant reduction when compared with the daytime values.

Echocardiographic characteristics

As shown in Table II, in the 106 subjects of the study left ventricular diameter and wall thickness values were close or slightly above the normality range (10,11), this being the case also for LVMI when calculated either in relation to body surface area or to height. The h/r ratio was close to the upper normality range values (with a trend towards

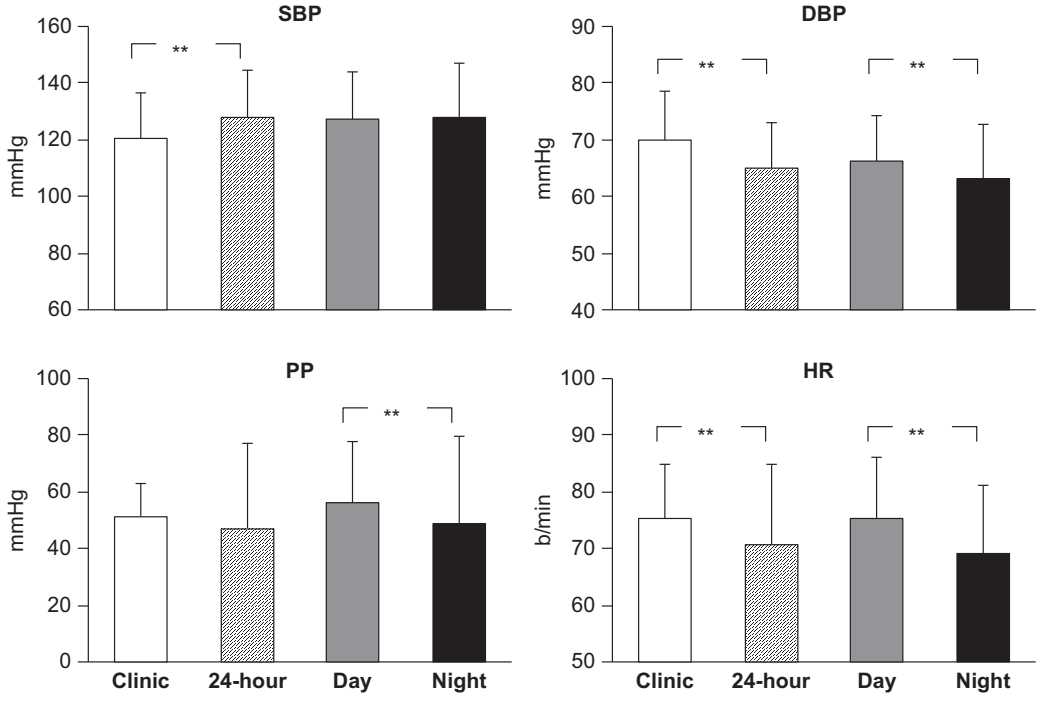

Figure 1. Systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP) and heart rate (HR) in 106 nonagenarian and centenarians subjects. Data are shown as means ± standard deviations. Asterisks (**$p < 0.01$) refer to the statistical significance between different values.

Table II. Echocardiographic characteristics of the whole population studied and of the two subgroups of normotensive (NT) and hypertensive (HT) subjects.

	All subjects ($n = 106$)	NT ($n = 45$)	HT ($n = 61$)
LV diastolic diameter (mm)	44.8 ± 3.7	44.1 ± 3.0	45.2 ± 4.1
LV septal wall thickness (mm)	10.8 ± 1.7	10.4 ± 1.7	11.0 ± 1.7
LV posterior wall thickness (mm)	10.1 ± 1.8	9.8 ± 1.3	10.4 ± 2.0
LVMI (g/m^2)	125.1 ± 31	120.7 ± 29	128.1 ± 33
LVMI ($g/height^{2.7}$)	55.9 ± 16	52.5 ± 18	58.3 ± 14
h/r	0.47 ± 0.08	0.46 ± 0.06	0.48 ± 0.09
E/A	0.88 ± 0.4	0.86 ± 0.3	0.90 ± 0.5
EF (%)	53.2 ± 4	54.0 ± 5	52.6 ± 3
Fractional shortening (%)	44.6 ± 11	48.8 ± 10	41.7 ± 12**
Atrial diameter (mm)	39.4 ± 6.0	37.2 ± 5	40.9 ± 7
Normal geometry (%)	16.3	19.1	12.7
Concentric remodelling (%)	23.3	27.7	19.6
Eccentric hypertrophy (%)	18.6	17.1	19.6
Concentric hypertrophy (%)	41.8	35.1	49.1

Data are shown as means ± standard deviations. Asterisks (**$p < 0.01$) refer to the statistical significance between normotensive (NT) and hypertensive (HT) subjects. LV, left ventricular; LVMI, left ventricular mass index; E/A, transmitral telediastolic (E) and protodiastolic (A) flow velocity ratio; h/r, left ventricular thickness/radius ratio; EF, ejection fraction.

concentric hypertrophy), and so was left atrial diameter, whereas left ventricular diastolic function, as assessed by the E/A ratio and the deceleration time, was clearly abnormal. With the exception of left ventricular diameter, all echocardiographic values (wall thickness, diameter, left atrium, E/A ratio, h/r ratio) were greater in subjects with than in those without a history of hypertension. Ejection fraction and fractional shortening values amounted to 53.2% and 44.6%, respectively.

Hypertensive vs normotensive subjects

As shown in Table I, female prevalence, serum creatinine and history of a cardiovascular event showed no significant difference between the two groups of subjects with and without a history of hypertension. Lipid variables and blood glucose also showed no significant difference between the two groups, although they were slightly higher in the hypertensive subjects. This was the case also for the values of echocardiographic variables, which in the hypertensive group were more clearly within the left ventricular concentric hypertrophy pattern (Table II). Clinic and ambulatory BP values were also higher in hypertensive than in normotensive patients (Figure 2), again with no nocturnal BP fall (data not shown). Clinic and ambulatory heart rate values were similar in the two groups (clinic heart rate: 74.4 ± 11.2 vs 76.3 ± 12.1 beats/min, ambulatory heart rate 69.2 ± 11.6 vs 69.2 ± 12.3 beats/min). Compared with treated hypertensive patients, untreated hypertensives showed, as expected, greater clinic and 24-h SBP and DBP values but not statistically different biochemical and echocardiographic variables (data not shown).

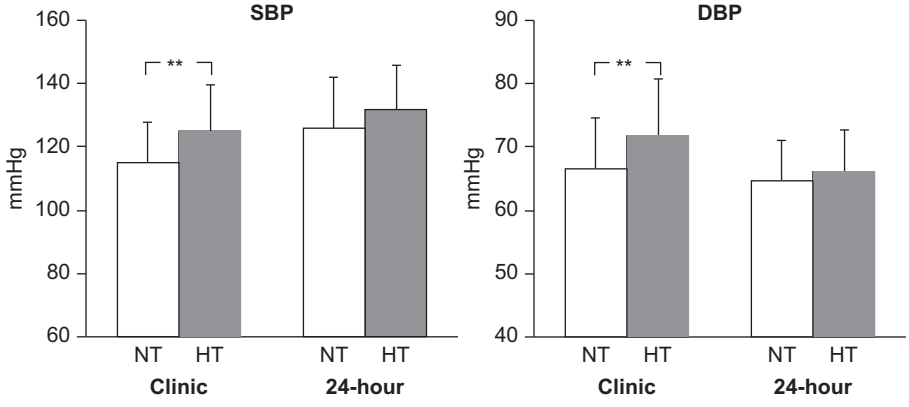

Figure 2. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) in normotensive (NT) and in hypertensive (HT) nonagenarian and centenarian subjects. Data are shown as means ± standard deviations. Asterisks (**$p < 0.01$) refer to the statistical significance between values recorded in the two groups.

Table III. Demographic, clinical and echocardiographic characteristics of nonagenarians and centenarians recruited in the study.

	Nonagenarians ($n = 89$)	Centenarians ($n = 17$)
Age (years)	94.0 ± 2.3	102.1 ± 2.0**
Female prevalence (%)	84.1%	94.1%
Body mass index (kg/m^2)	22.2 ± 4.3	21.9 ± 2.9
Total cholesterol (mg/dl)	171.2 ± 39.1	174.3 ± 30.6
Triglycerides (mg/dl)	106.0 ± 43.4	136.3 ± 47.7
HDL-cholesterol (mg/dl)	44.5 ± 15.4	40.0 ± 9.4
Blood glucose (mg/dl)	88.6 ± 23.4	88.5 ± 16.4
Serum creatinine (mg/dl)	1.1 ± 0.4	1.0 ± 0.4
Glomerular filtration rate (ml/min)	33.2 ± 14.9	28.0 ± 5.0
Clinic SBP/DBP (mmHg)	121.8 ± 15.6/70.1 ± 8.9	115.3 ± 17.0/67.7 ± 8.3
24-h SBP/DBP(mmHg)	128.9 ± 16.6/64.8 ± 8.2	124.3 ± 14.7/65.2 ± 7.3
Clinic HR (beats/min)	75.4 ± 9.7	75.2 ± 11.2
24-h HR (beats/min)	71.3 ± 11.1	68.6 ± 22.8
LVMI (g/m^2)	123.8 ± 43.1	131.9 ± 28.1
LVMI (g/height$^{2.7}$)	55.4 ± 20.4	58.8 ± 13.2
E/A	0.87 ± 0.59	0.94 ± 0.44
EF (%)	53.4 ± 5.0	51.7 ± 7.7
Atrial diameter (mm)	38.7 ± 7.4	43.5 ± 10.3*

Data are shown as means ± standard deviations. Asterisks (**$p < 0.01$, $p < 0.05$) refer to the statistical significance between nonagenarians and centenarians. HDL, high-density lipoprotein; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; LVMI, left ventricular mass index; E/A, transmitral telediastolic (E) and protodiastolic (A) flow velocity ratio; EF, ejection fraction.

Nonagenarians vs centenarians

As shown in Table III, in centenarians, triglyceride, LVMI and left atrial diameter values were greater than in nonagenarians, whereas glomerular filtration rate and clinic and 24-h BP values were lower. With the exception of left atrial diameter value, none of the above difference achieved, however, statistical significance.

Correlations

There was a significant, although weak, correlation between clinic and 24-h SBP and DBP ($r = 0.30$ and $r = 0.34$, $p < 0.01$). For either clinic and ambulatory BP, the SBP values showed a significant correlation with DBP ($r = 0.31$ and $r = 0.28$, $p < 0.001$ for both). Both when quantified by body surface area and by height, LVMI showed a significant relationship with SBP and pulse pressure but not with DBP, the correlation coefficients being somewhat closer for 24-h than for clinic values [24-h vs LVMI (g/m^2) $r = 0.24$ and $r = 0.23$, $p < 0.04$; 24-h vs LVMI (g/h$^{2.7}$) $r = 0.22$ and $r = 0.21$, $p < 0.05$; clinic vs LVMI (g/m^2) $r = 0.20$ and $r = 0.22$, $p < 0.05$; 24-h vs LVMI (g/h$^{2.7}$) $r = 0.20$ and $r = 0.21$, $p < 0.05$]. No correlation was observed between E/A ratio or deceleration time and BP. In a multivariate analysis, ambulatory but not clinic BP was an independent determinant of LVMI values after age and before body mass index and blood glucose values.

Discussion

The present study represents one of the largest reports examining in nonagenarian and centenarian subjects the BP and cardiac structural and functional alterations characterizing very advanced age strata. Confirming previous findings by our group and others (1,3–5), our study shows that in subjects with an age greater than 90 years, clinic DBP values are higher than ambulatory DBP and that during the night-time period the physiological BP reduction seen at younger age is markedly attenuated. It adds to these data three pieces of new information, i.e. the evidence that in nonagenarians and centenarians: (i) 24-h ambulatory SBP values are greater for magnitude than the corresponding clinic values; (ii) left ventricular hypertrophy (particularly of concentric type) is frequently detected, this being the case also for left ventricular diastolic dysfunction; and (iii) at the multivariate analysis, age and, to a lesser extent, ambulatory BP load appear to be involved in determining the structural changes detectable by the echocardiographic technique at the level of the left ventricle. This allows three conclusions to be drawn: (i) the pressor response (particularly SBP) to sphygmomanometric BP measurement appears to be attenuated when the patient's age is close to 100 years; (ii) cardiac structural alterations of the left ventricle are a common finding in nonagenarians and centenarians, affecting on the whole about 70% of the population sample of the present study; and (iii) in both normotensive and essential hypertensive individuals, age represents a factor likely to be involved in determining the structural alterations affecting the left ventricle.

It has been previously reported that office BP values are significantly higher than daytime BP in centenarians than in octogenarians, thereby suggesting that the prevalence of the white coat effect is greater

in the former than in the latter group (12). At first glance, our results are not in line with these findings, since they show that in our subjects clinic SBP values are lower than the corresponding ambulatory ones. It should be noted, however, that when the comparison was made between clinic and daytime DBP values, a tendency of the former to be higher than the latter was detectable also in our population sample. Thus our findings suggest that in nonagenarians and centenarians, a white coat effect is not necessarily detectable, or if present, it quite selectively affects, in a markedly attenuated fashion, DBP only. This attenuation may be explained considering that subjects in the very advanced age decades display a reduced pressor response to a variety of laboratory manoeuvres, which, such as the alerting reaction to BP measurement (13), represent stressful stimuli (14). It may be also explained, however, by taking into account the different characteristics of the populations examined in the study by Jumabay and coworkers (12), which, at variance from ours, enrolled centenarians free from major disease and without any pharmacological treatment. The presence of both these factors in our population may have indeed interfered with the cardiovascular, and particularly BP, responses to the white coat effect.

Several other results of our study deserve to be briefly discussed. First, our population study has a cross-sectional nature that makes clarification of the mechanisms responsible for the presence of echocardiographic alterations in the very elderly population difficult. However, the evidence that at a multivariate analysis age represents the factor more closely related to LVMI may allow us to advance the hypothesis that the aging factor is of some relevance for determining alterations in cardiac structure even when BP values of the subjects are in the high BP range. This is in part confirmed by the evidence that in our population the concentric type of hypertrophy prevailed over the eccentric one, known to be common in essential hypertension (15,16). Second, confirming previous findings, in our nonagenarian and centenarian individuals there was an attenuation of the physiological fall in BP (particularly SBP) occurring during the night-time period (3–5). This alteration may depend on the loss of the sleep-dependent ability to reduce sympathetic cardiovascular drive (17,18). Whether this reduction is accompanied by a similar decrease in vagal control of heart rate, however, is more difficult to be determined, given the evidence that, at variance from previous findings from our group (3), in the present study we found in our nonagenarians and centenarians a preservation of the sleep-dependent heart rate reduction.

The present study has a number of limitations. First, we studied patients with previous history of cardiovascular disease or treated with antihypertensive drugs, which may have affected the observed data. Second, the measurements we performed did not include night-time electroencephalography, oculographic and electromyographic recordings, thus preventing us in providing an undisputed demonstration of the absence of any interference of the BP monitoring with the sleep process. The lack of these data also prevented a proper evaluation of the behaviour of BP during different sleep stages. Finally, measurements of night-time BP values during sleep every 20 min may have interfered with the occurrence of the dipping BP profile.

Declaration of interest: The authors declare that there is no conflict of interest.

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