Non-Dipping Pattern and Subclinical Cardiac Damage in Untreated Hypertension: A Systematic Review and Meta-Analysis of Echocardiographic Studies

Cesare Cuspidi,1,2 Carla Sala,3 Marijana Tadic,4 Marta Rescaldani,3 Guido Grassi,1,5 and Giuseppe Mancia2

AIM
The association of non-dipping (ND) pattern with cardiac damage is debated. We performed a meta-analysis in order to provide comprehensive information on subclinical cardiac alterations in untreated ND hypertensives.

DESIGN
A computerized search was performed using PubMed, OVID, EMBASE, and Cochrane library databases from 1 January 1990 up to 31 October 2014. Full articles published in English language providing data on subclinical cardiac damage in ND as compared to dipper (D) hypertensives, as assessed by echocardiography, were considered.

RESULTS
A total of 3,591 untreated adult subjects (1,291 ND and 2,300 D hypertensives) included in 23 studies were considered. Left ventricular (LV) mass index (LVMI) was higher in ND than in D hypertensives (122 ± 3.8 g/m² vs. 111 ± 3.3 g/m², standardized mean difference, SMD: 0.40 ± 0.07, confidence interval (CI): 0.26–0.53, P < 0.001); relative wall thickness (RWT) and left atrium (LA) diameter were greater (SMD: 0.14 ± 0.005, CI: 0.05–0.23, P = 0.002; 0.36 ± 0.10, CI: 0.16–0.56, P < 0.001, respectively), while mitral E/A ratio was lower in ND than in D counterparts (SMD: −0.23 ± 0.08, CI: −0.39 to −0.08, P = 0.003). After assessing data for publication bias, the difference between groups was still significant, with the exception of E/A ratio.

CONCLUSIONS
Our meta-analysis supports an association between ND pattern and increased risk of LV structural alterations in untreated essential hypertensives. This observation supports the view that an effective BP control throughout the entire 24-hour cycle may have a key role in preventing or regressing subclinical cardiac damage associated to ND pattern.

Keywords: blood pressure; essential hypertension; hypertension; non-dipping; subclinical cardiac damage.

doi:10.1093/ajh/hpv094

A consistent body of evidence supports the view that 24-hour ambulatory blood pressure monitoring (ABPM) by providing a large number of blood pressure (BP) readings during daily life is superior to office BP in the diagnostic and prognostic assessment of hypertensive subjects.1 In particular, ABPM offers the unique opportunity to evaluate day–night BP variability: day-time values, due to reduced sympathetic and increased vagal tone during nocturnal bed-rest period, leading to a marked decrease in heart rate, cardiac output, and peripheral resistances. Numerous studies have shown that nor-epinephrine and epinephrine levels have circadian variations with a nadir during night-time sleep. The pathogenetic mechanism of impaired BP decline is multifactorial. The non-dipping (ND) pattern has been documented to be highly prevalent in a variety of conditions including secondary hypertension, chronic renal diseases, diabetes mellitus, sleep-apnea syndrome, autonomic nervous system dysfunction, and pregnant women with pre-eclampsia.3 A blunted nocturnal decline in sympathetic tone and renin-angiotensin-aldosterone system activity, an impaired renal capacity to excrete sodium and endothelial dysfunction have been linked to ND pattern.

In the last decades, the increasing use of ABPM for clinical and research purposes has documented that the majority of essential hypertensive patients exhibit a marked nocturnal fall in BP during sleep (dipping pattern). On the other hand,
a reduced or even absent night-time BP decrease has been shown to occur in a noticeable fraction of the hypertensive population (20–40%), regardless of ethnic, age, gender, and body size characteristics (ND pattern).\(^7,8\) ND as opposed to dipping pattern (D) has been reported to affect adversely subclinical markers of cardiac and extra-cardiac hypertensive organ damage and cardiovascular prognosis.\(^9,10\) This finding may be related to the fact that hypertensive patients exposed to pressure overload in the nocturnal period develop more extensive cardiovascular damages than those exposed to a lower pressure load during sleeping hours.

Unfortunately, the clinical and prognostic value of ND pattern is still debated, as a number of studies failed to demonstrate significant differences in target organ damage and cardiovascular outcomes between dipper and non-dipper hypertensives with similar 24-hour BP values.\(^11\) In particular, it has been recently suggested that average nocturnal BP levels are better associated with subclinical organ damage and incident cardiovascular events as compared to percent nocturnal BP decrements from day-time values.\(^12,13\)

Considering the conflicting results of available literature and the lack of an updated systematic analysis on this issue, we performed a meta-analysis to investigate whether ND pattern in untreated essential hypertensive patients is a risk factor for morphological and functional ultrasonographic alterations of the heart.

**METHODS**

**Search strategy and study selection**

The present study was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines.\(^14\)

Medical literature was reviewed in order to identify all articles evaluating the association of ND pattern with subclinical cardiac damage (i.e., left ventricular (LV) mass) as assessed by echocardiography.

A computerized search was performed using PubMed, OVID, EMBASE, and Cochrane library databases from 1 January 1990 up to 31 October 2014. Studies were identified by crossing the following search terms: “non-dipping,” “reduced nocturnal BP fall,” “circadian BP variation,” “night-time BP” with “hypertension” “cardiac damage,” “left ventricular mass,” “left ventricular hypertrophy,” “cardiac dysfunction,” “echocardiography.” Checks of the reference lists of selected papers and pertinent reviews complemented the electronic search. Data were extracted by 2 independent investigators (C.C. and C.S.), and additional data were obtained by personal contact with authors of selected papers.

Specific inclusion criteria were: (i) full articles published in English in peer-reviewed journals; (ii) studies reporting data on at least one of the following continuous variables: average LV mass index (LVMI), relative wall thickness (RWT), left atrium (LA) size, LV diastolic parameters (and SD) as assessed by echocardiography in 10 or more untreated adult ND essential hypertensives; (iii) minimum data set including age, gender, and average ABPM values (at least one of the following: average 24-hour, day-, or night-time values).

Studies including patients on antihypertensive medications, with secondary hypertension, chronic kidney disease, or renal transplant recipients were excluded. Only updated or largest reports were considered when multiple publications by the same research group were found in order to avoid double counting subjects.

The first literature search identified 960 papers. After the initial screening of titles and abstracts, 850 studies were excluded as they did not address the relation between ND and cardiac organ damage and 110 were reviewed; of these, 23 studies fulfilled the inclusion and exclusion criteria and contained sufficient clinical and echocardiographic data to be included in the final review\(^15–37\) (Figure 1).

![Figure 1. Schematic flowchart for the selection of studies.](https://academic.oup.com/ajh/article-abstract/28/12/1392/153524)
Study quality evaluation

Two independent reviewers (C.C. and C.S.) graded each study evaluating the following items: (i) office BP measured in 2 or more sessions vs. a single session; (ii) use of validated ABPM devices; (iii) definition of nocturnal BP patterns based on 2 ABPM sessions or 48-hour BP recording; (iv) blind assessment of echocardiographic examinations; (v) sample study including at least 30 cases and controls in order to detect at least a 10% difference between groups in echocardiographic variables; (vi) study based on case–control design, (vii) statistical adjustment for covariates such as age, body mass index, and 24-hour ambulatory BP. According to this evaluation score, quality was arbitrarily classified as poor (0–2 points), fair (3–4 points), good (5–6 points), and excellent (7 points).

Statistical analysis

The primary aim of meta-analysis was to compare echocardiographic alterations in LV structure and function expressed as continuous variables, i.e., LVMI, RWT, LA diameter, the ratio of early (E) to late (A) peak of mitral inflow velocity (E/A ratio) in ND as compared to D hypertensives. To this purpose, a pooled analysis of cardiac parameters was performed using fixed or random effects meta-analysis by Comprehensive Meta-Analysis Version 2, Biostat, Englewood, NJ. Standardized mean difference (SMD) with the 95% confidence interval (95% CI) was used to calculate the statistical difference of the above-mentioned continuous variables between dippers and non-dippers.

Demographic and clinical data provided by selected studies are expressed as absolute numbers, percentage, mean ± SD. As 3 of 23 studies provided the association between ND and cardiac variables separately in men and women without providing pooled data, they were analyzed as separate studies. Meta-regression analysis was used to test the linear relationship between LVMI (and other markers of cardiac damage) and continuous explanatory variables such as clinic or ambulatory BP.

Statistical significance was set at \( P < 0.05 \).

Heterogeneity was estimated using the \( I^2 \) test; random effect models were applied when heterogeneity across studies was high (\( I^2 > 75 \)). Publication bias was assessed by using the funnel plot method.

RESULTS

Characteristics of the studies

Table 1 shows the main characteristics of analyzed studies, including, sample size, mean age, gender distribution, mean body mass index, office systolic and diastolic BP, mean 24-hour, and day-time and night-time BP values in ND hypertensives.

Overall, 3,591 untreated hypertensive subjects (ND = 1,291, D = 2,300) of both genders were included in 23 studies (sample size range 10–149 ND and 10–413 D participants) performed in 3 different geographical areas (Europe = 14; Asia = 8; North America = 1). Of note, the vast majority of the population (75.5%) was examined in Europe.

Echocardiographic assessment of cardiac structural and functional changes associated to ND pattern was the primary aim of all studies but two.19,37 All subjects had been recruited from departments of Medicine16,18–20,22–29,31,34 or Cardiology30,32,33,35,37 and from out-patient hypertension clinics.15,17,21,36

Data on study quality evaluation

The score of each article ranged from 3 (fair quality) to 6 (good quality). One study had a score of 3,18 14 studies \( 4,2,5,6,8–10,12–16,19–21 \) 6 studies 5 points,1,3,7,11,17,23 and 2 studies 6 points4,22 (Table 1). Inter-observer reproducibility in evaluating the quality of studies was 91%.

Blood pressure measurements and definition of dipping/ non-dipping status

Brachial clinic BP was measured according to the recommendations of international/national guidelines (data provided by 16 of 23 studies). Mercury sphygmomanometer was used in 10 studies and electronic device in 1 study20; the remaining studies did not provide any information on the device. Of note, clinic BP was determined by taking multiple measurements during at least 2 visits in 11 studies.16,18,20–24,29,31,34,36

Ambulatory BP was measured on the non-dominant arm by using validated devices in all studies. Spacelabs 5200, 90202, 90207 (Spacelabs, Redmond, WA) were the more frequently used devices (8 studies), followed by Takeda (AND) TM 2420, 2421, 2425, 2430 (Tokyo, Osaka, Asashi, Japan) (6 studies). Instruments were set to take BP readings at different time intervals (15–30 minutes during daytime and 20–60 minutes during nighttime).

Patients were defined as non-dippers when nighttime systolic and diastolic BP (19 studies), systolic BP18,28 and mean BP16,30 decreased ≤10% compared to day-time values.

Night-time period was defined according to 8 different criteria (data from 22 studies). Time interval from 11.00 pm to 7.00 am was the most frequently used20,21,24,32,35,38 followed by the interval from 12.00 pm to 6.00 am27,29,30,34,37 and from 10.00 pm to 6.00 am13,18,26,28 Day-active and night-rest periods were defined according to individual’s diary in 3 studies19,22,31 and by an actigraphy device in 1.17 Wide and narrow fixed night-time periods were used in 1315,16,18,20,21,24–26,28,32,33,35,36 and 5 studies,27,29,30,34,37 respectively.

Clinical characteristics of ND hypertensive subjects

All ND subjects included in selected studies were free of clinical or laboratory evidence of heart failure, coronary heart disease, valve defects, or secondary causes of hypertension. Mean age range was 41–72 years,21,27 55% of participants were men (n = 705). Average BMI ranged from...
Table 1. Summary of echocardiographic studies reporting data on subclinical cardiac damage in untreated non-dipping essential hypertensive subjects

<table>
<thead>
<tr>
<th>Author</th>
<th>Reference</th>
<th>Sample size (n)</th>
<th>Age (years)</th>
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<th>Office SBP/DBP (mm Hg)</th>
<th>Mean 24-hour SBP/DBP (mm Hg)</th>
<th>Mean day-time SBP/DBP (mm Hg)</th>
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</table>

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; n.a., not available; QS, quality score (see text); SBP, systolic blood pressure.

*Data are shown as absolute numbers, percentages, means ± SD or SE.

23.0 ± 3.0 kg/m² to 30.7 ± 4.0 kg/m² (data provided by 19 studies, 1,032 subjects).

Average night-time systolic BP varied from 114 ± 10 mm Hg to 150 ± 7 mm Hg and diastolic BP from 70 ± 5 mm Hg to 96 ± 6 mm Hg.

Clinical characteristics of D hypertensive subjects

Prevalence of men in D hypertensive subjects was 51% (n = 1,184). Mean age ranged from 39 ± 20 to 70 years and mean BMI from 22.0 ± 3.0 kg/m² to 30.7 ± 4.0 kg/m² (Table 2). Average night-time systolic BP ranged from 115 ± 12 mm Hg to 142 ± 27 mm Hg and night-time diastolic BP from 66 ± 5 mm Hg to 88 ± 17 mm Hg.

Echocardiographic findings in ND and D hypertensive subjects

LV diameters and wall thickness were measured by M-mode technique (in almost all instances under 2-dimensional control) in all studies according to ASE15–19,22,25–34,37 or PENN20–24,35,36 convention. LV mass was calculated in all studies using necropsy-validated equations.

In all selected studies but 2,20,25 LVM was normalized to body surface area. In the pooled study population, mean LVM ranged from 90 g/m² to 156 g/m² in ND hypertensive subjects and from 82 g/m² to 153 g/m² in their D counterparts.

Mean LVM was 121.6 ± 3.8 g/m² in ND hypertensives and 110.9 ± 3.3 g/m² in D ones.
<table>
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<th>Age (years)</th>
<th>Men (%)</th>
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<td>413</td>
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<td>n. a.</td>
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Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; n.a., not available; SBP, systolic blood pressure.

*Data are shown as absolute numbers, percentages, means ± SD or SE.*
Figure 2 reports the SMD of LVMI in 2,201 ND and 1,230 D hypertensives: the value was positive in favor of ND individuals (0.40 ± 0.07, CI: 0.26–0.53, \( P < 0.001 \)). Pooled data from 15 studies\(^{16,17,20,21,23–25,27,29,32,34–37}\) documented that RWT (an index reflecting the type of LV geometry) was 0.41 ± 0.007 in ND (\( n = 1,185 \)) and 0.40 ± 0.014 in D hypertensives (\( n = 805 \)) with an SMD of 0.14 ± 0.005, CI: 0.05–0.23, \( P = 0.002 \) (Figure 3).

Data from 10 studies\(^{20,22,23,27–29,32,34–36}\) showed that LA diameter was 36.0 ± 0.6 mm in ND (\( n = 587 \)) and 34.2 ± 0.98 mm in D (\( n = 459 \)) subjects; SMD was 0.36 ± 0.10, CI: 0.16–0.56, \( P < 0.001 \) (Figure 4).

As for LV diastolic function, as assessed by E/A ratio, the average value from 10 studies\(^{20,21,23,25,28,30,34–37}\) was 0.98 ± 0.05 in ND (\( n = 779 \)) and 1.02 ± 0.05 in D individuals (\( n = 558 \)) (SMD = −0.23 ± 0.08, CI: −0.39 to 0.08, \( P = 0.003 \)) (Figure 5).

A funnel plot (trim and fill test) excluded the presence of relevant publication bias of studies comparing LVMI in ND and D hypertensives. Adjustment for publication bias attenuated but not abolished the difference in LVMI (SMD: 0.24, CI: 0.09–0.39, \( P < 0.01 \)), as well as in RWT (SMD: 0.13, CI: 0.05–0.23, \( P = 0.006 \)), and LA diameter (SMD: 0.25 CI: 0.03–0.47, \( P < 0.01 \)) between groups. Adjustment for publication bias abolished the difference in E/A ratio between D and ND (SMD: 0.15, CI: −0.04 to +0.33, \( P = 0.07 \)).

A sensitivity analysis showed that the final result was not substantially affected by a single study effect.

Additional analyses, restricted to LVMI, as data concerning this cardiac phenotype were provided by all studies were performed in subgroups divided by geographical area (European vs. non-European), definition of dipping/ND according to a single or 2 ambulatory BP sessions wide and narrow fixed night-time periods. LVMI was higher in ND independently from geographical area and definition of ND based on single or 2 ABPM recordings. Finally, LVMI resulted to be significantly higher in ND defined by wide but not by narrow fixed night-time periods (data not shown).

**Correlation analyses**

A meta-regression analysis of data from ND hypertensives (\( n = 1,053 \)) showed that LVMI was significantly correlated with average daytime systolic BP (slope 1.68, \( P = 0.002 \)), night-time systolic BP (slope 2.38, \( P = 0.003 \)), day-time diastolic BP (slope 1.82, \( P = 0.02 \)), night-time diastolic BP (slope 1.84, \( P = 0.02 \)), and clinic systolic BP (slope 1.59, \( P = 0.02 \)). In the pooled population (\( n = 3,011 \)), the absolute difference between day and night diastolic BP tended to correlate with...
Figure 3. Forest plot for unadjusted standardized mean difference (SMD) of relative wall thickness in non-dipper (n = 1,185) and dipper (n = 805) hypertensive patients (random model, P = 0.002). Abbreviation: CI, confidence intervals.

Figure 4. Forest plot for unadjusted standardized mean difference (SMD) of left atrial diameter in non-dipper (n = 587) and dipper (n = 459) hypertensive patients (random model, P < 0.001). Abbreviation: CI, confidence intervals.
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LVMI (slope 0.99, \(P = 0.06\)); this was not the case for the absolute difference of systolic BP (slope 0.29, \(P = 0.43\)).

DISCUSSION

The present meta-analysis of 23 studies published since 1995 provides a comprehensive and updated information on subclinical cardiac damage, as assessed by echocardiography, in a pooled population of 1,291 untreated uncomplicated essential hypertensive subjects with a reduced nocturnal BP decline (non-dippers) as compared to 2,300 dipper individuals. The main findings of our study were the following: (i) LVMI, RWT, and left atrial diameter were higher in ND than in D hypertensives; (ii) E/A ratio was reduced in ND as compared to their D counterparts; (iii) differences in cardiac structure were unaffected by the presence of a publication bias or by a single study effect, this was not also the case for E/A ratio. Several important aspects of our results deserve to be further commented.

Echocardiographic markers of subclinical cardiac damage, such as LV hypertrophy (LVH), concentric geometry, LA enlargement and impaired diastolic function, have been shown to predict the risk of incident cardiovascular disease in essential hypertensives, as well as in a variety of clinical settings, independently from BP levels, conventional and emerging risk factors.

In particular LVH, a cardinal manifestation of hypertensive target organ damage, represents an integrated marker of cardiovascular risk, reflecting the impact of several risk factors on the heart. The magnitude of cardiovascular risk associated to LVH in a population depends on clinical/demographic characteristics as well as on diagnostic tools (echocardiography vs. electrocardiography) used to detect this condition. In the Pressioni Monitorate e Loro Associazioni study, individuals with echocardiographic LVH exhibited an approximately 3-fold greater risk of cardiovascular mortality compared to subjects with normal LV mass.

Our analysis underlines that ND hypertensives have a greater prevalence of LVH and other abnormal echocardiographic phenotypes, such as concentric geometry, LA enlargement, and diastolic dysfunction. Of note, these markers of subclinical cardiac damage in ND, persisted to be statistically significant after adjustment for publication bias, with the exception of E/A ratio. This last finding may be related either to the fact that LV diastolic function was preserved in newly diagnosed untreated ND hypertensives or, more likely, to the limited sensitivity of E/A ratio in detecting subtle alterations in LV relaxation as compared to other techniques, such as tissue Doppler imaging.

Studies including patients on antihypertensive medications were excluded from our meta-analysis as drug treatment is known to affect the relationship between BP and organ damage. It has been consistently shown, indeed, that angiotensin receptor antagonists, angiotensin-converting-enzyme inhibitors, calcium antagonists are more effective than other classes of drugs in reducing LVMI, in front of similar office or out-of-office BP lowering effects.

Conflicting findings in the existing literature on the association between circadian BP variations and target organ damage are mostly related to the impact of clinical and methodological variables. In the attempt to prevent potential interferences, we focused our analysis on untreated
hypertensive subjects, free of overt cardiovascular disease, type 2 diabetes, and other relevant comorbidities impacting on day–night BP variations.

Among the studies included in our meta-analysis as many as 8 different criteria were adopted to classify night-time and day-time periods. Heskens et al.35 showed that definition of awake–asleep time by different criteria (wide or narrow fixed night-time periods or effective nocturnal bed-rest time as assessed by patient’s diary) significantly affected the magnitude of BP fall, the classification of ND and D individuals and consequently the extent of organ damage associated to ND pattern.

Several definitions of ND status have been proposed based on isolated systolic, diastolic, or combined systolic and diastolic nocturnal BP fall. The majority of selected studies (19 of 23) defined ND according to both BP components. Syrseloudis et al.36 investigated that the prevalence of cardiac extra-cardiac organ damage in 279 untreated essential hypertensives was according to different definitions of ND pattern. They found that systolic ND, as compared to diastolic or systolic-diastolic ND, was associated with higher LVMI, urinary albumin excretion rate, and arterial stiffness. The dominant role of systolic nocturnal BP in determining new-onset LVH was also demonstrated by our group in the Pressioni Monitorate e Loro Associazioni population.47

Classification of ND and D status has been shown to have a limited reproducibility over time in essential hypertensives. As a consequence, categorization of ND pattern based on a single ABPM may not accurately reflect this BP phenotype in a noticeable fraction of the hypertensive population, ranging from 20 to 35%.48,49 Unfortunately, only 4 of 23 studies19,22,31,36 included in this meta-analysis identified nocturnal BP patterns based on 2 ABPM sessions.

Some additional points merit to be further discussed in order to offer detailed information in this important issue.

A meta-analysis by Fagard et al.,30 involving 1,223 normotensive and hypertensive participants (29% untreated), indicated that LV mass had a non-different correlation coefficient with night-time and day-time systolic BP. Our meta-regression analyses, in keeping with these results, showed significant correlations between LVMI and systolic BP values, either during daytime and nighttime, in ND hypertensive patients. In addition, our meta-analysis documented that LVMI tended to be higher (P = 0.06) in patients with the smallest fall in day–night diastolic BP; this was not the case for systolic BP fall. A possible explanation for this finding faces with the role of increased peripheral resistances in determining cardiovascular alterations in young, middle aged, hypertensive subjects, which represented the vast majority of the pooled population.

It has been reported that night-time BP levels have a better prognostic value than ND status. In particular, in a large population-based meta-analysis including 25,856 hypertensive patients and 9,641 individuals randomly recruited from populations, night-time BP was a better predictor of outcomes than day-time, day-night BP ratio, and the extent of nocturnal BP decline.51 Emerging evidence supports the view that the adverse clinical significance of dipping/ND classification is related to the absolute levels of nocturnal BP. In the Pressioni Monitorate e Loro Associazioni population the absolute levels of night-time systolic BP rather than the extent of nocturnal systolic blood pressure declines predicted new-onset LVH.47 As the likelihood of having elevated absolute nocturnal BP levels is higher in non-dippers than in dippers, ND status should be regarded as a marker of increased cardiovascular risk. In a clinical perspective, a comprehensive evaluation of nocturnal BP in hypertensive patients should take into account mean night-time BP rather than the extent of BP fall at night.

Several limitations of the current meta-analysis need to be mentioned. First, all studies included in the present review had a cross-sectional design, thus, any cause–effect between ND pattern and cardiac damage should be considered hypothetical. According to current interpretation, a reduced nocturnal BP fall should promote organ damage in hypertension, although the alternative explanation that an adequate BP fall during sleep only occurs when cardiovascular structure is preserved, should be considered.32 Second, different definitions of abnormal nocturnal BP fall (systolic, systolic-diastolic, or mean BP) as well as of day-time and night-time periods were used to classify dippers and non-dippers. The different classifications of the ND phenotype may have influenced our results. Third, our findings were limited to untreated, uncomplicated hypertensive subjects; thus, they should not be extended to different clinical settings such as treated or secondary hypertension, diabetic subjects or patients with chronic renal disease. Fourth, it is worth noting that we did not analyze the original database, but only the results derived from revised manuscripts. Finally, our analysis was restricted to papers published in English due to difficulties in retrieving and interpreting papers in other languages. This linguistic restriction may have affected our results.53

Available evidence on the relationship between ND pattern and subclinical cardiac damage is mostly based on results provided by single small-scale studies. The present meta-analysis examining a large pooled population of ND subjects adds further information in this area by showing that echocardiographic alterations of cardiac structure are more pronounced in ND than in D essential hypertensives. In a practical perspective, this observation supports the view that an effective BP control throughout the entire 24-hour cycle may have a key role in preventing or regressing subclinical cardiac damage in hypertensive patients. Chrono-therapy represents a promising way to reduce nocturnal hypertension and restore a normal circadian BP rhythm. Emerging evidence has shown that bedtime dosing of antihypertensive medication reduces nocturnal BP and increases day-night BP fall more than standard morning dosing and, more importantly, reduces cardiovascular morbidity and mortality.54

DISCLOSURE

The authors declared no conflict of interest.

REFERENCES

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