Prognostic Effect of the Nocturnal Blood Pressure Fall in Hypertensive Patients

The Ambulatory Blood Pressure Collaboration in Patients With Hypertension (ABC-H) Meta-Analysis

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Abstract—The prognostic importance of the nocturnal systolic blood pressure (SBP) fall, adjusted for average 24-hour SBP levels, is unclear. The Ambulatory Blood Pressure Collaboration in Patients With Hypertension (ABC-H) examined this issue in a meta-analysis of 17 312 hypertensives from 3 continents. Risks were computed for the systolic night-to-day ratio and for different dipping patterns (extreme, reduced, and reverse dippers) relative to normal dippers. ABC-H investigators provided multivariate adjusted hazard ratios (HRs), with and without adjustment for 24-hour SBP, for total cardiovascular events (CVEs), coronary events, strokes, cardiovascular mortality, and total mortality. Average 24-hour SBP varied from 131 to 140 mm Hg and systolic night-to-day ratio from 0.88 to 0.93. There were 1769 total CVEs, 916 coronary events, 698 strokes, 450 cardiovascular deaths, and 903 total deaths. After adjustment for 24-hour SBP, the systolic night-to-day ratio predicted all outcomes: from a 1-SD increase, summary HRs were 1.12 to 1.23. Reverse dipping also predicted all end points: HRs were 1.57 to 1.89. Reduced dippers, relative to normal dippers, had a significant 27% higher risk for total CVEs. Risks for extreme dippers were significantly influenced by antihypertensive treatment ($P<0.001$): untreated patients had increased risk of total CVEs (HR, 1.92), whereas treated patients had borderline lower risk (HR, 0.72) than normal dippers. For CVEs, heterogeneity was low for systolic night-to-day ratio and reverse/reduced dipping and moderate for extreme dippers. Quality of included studies was moderate to high, and publication bias was undetectable. In conclusion, in this largest meta-analysis of hypertensive patients, the nocturnal BP fall provided substantial prognostic information, independent of 24-hour SBP levels. **(*Hypertension*. 2016;67:693-700. DOI: 10.1161/HYPERTENSIONAHA.115.06981.)** ● **Online Data Supplement**

Key Words: blood pressure ■ blood pressure monitoring, ambulatory ■ hypertension ■ meta-analysis ■ publication bias

Ambulatory blood pressure (BP) monitoring (ABPM) has been increasingly used in clinical management of hypertension.[1,2] It has been consistently demonstrated that ambulatory 24-hour BPs are better cardiovascular risk predictors than office BPs[2,3] and that average nighttime sleep BPs are generally better predictors of adverse cardiovascular outcomes than average daytime awake BP levels on ABPM.[2,4,5] There is a normal circadian BP variability, with higher levels during daytime and a 10% to 20% BP fall during sleep.[2] In 1988, O'Brien et al[6] reported for the first time that hypertensives with a blunted nocturnal BP fall had a greater prevalence of strokes and named these patients nondippers, in contrast to the normal dippers. Since then, several prospective studies reported on the prognostic value of the nocturnal BP fall both in hypertensives[7–18] and in population-based samples.[19–21] However, these results were not consistent possibly because of differences in methodology, study populations, sample sizes, and end points.[9] In particular, many previous studies either did not adjust the

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analyses for average 24-hour BP levels or did not examine the nocturnal BP fall as a continuous variable (the night-to-day BP ratio) or did not evaluate the different subgroups of abnormal dipping pattern (eg, the extreme dippers or the reverse dippers). These aspects also have not been comprehensively addressed in previous meta-analyses.[4,5,9,10]

Therefore, the Ambulatory Blood Pressure Collaboration in Patients With Hypertension (ABC-H),[5,22] as far as we know the largest cohort-level meta-analytic ABPM database with 17 312 hypertensive individuals from 3 continents, aimed to comprehensively assess the prognostic effect of several nocturnal BP fall parameters for cardiovascular morbidity and mortality outcomes. In particular, we addressed whether the nocturnal BP fall still retained its prognostic value after simultaneous adjustment for ambulatory average 24-hour BP levels and whether different abnormal nocturnal BP fall patterns (extreme dippers, reduced dippers, and reverse dippers) had independent prognostic value in contrast to the normal dipping pattern.

Methods

The ABC-H enrolled 7 cohorts from Europe (Belgium and Europe[9,10]; Perugia, Italy[8,17]; Pescara and Chieti, Italy[11]; Terrassa, Spain[18]; Vigo, Spain[16]; Porto, Portugal[15]; and United Kingdom and Ireland[12]), 1 cohort from South America (Rio de Janeiro, Brazil[14]), and 2 cohorts from Asia (Hyogo, Japan[7]; and Saga, Japan[13]), totaling 10 cohorts and 17 312 hypertensive patients. The nocturnal BP fall was assessed by 3 different parameters: (1) the continuous systolic night-to-day ratio (SBP-NDR); (2) the traditional dipping/nondipping groups, defined as a SBP-NDR ≤0.9 and >0.9, respectively; and (3) the 4 categories of dipping: normal dippers (SBP-NDR, ≤0.9 and >0.8), extreme dippers (SBP-NDR, ≤0.8), reduced dippers (SBP-NDR, >0.9 and ≤1.0), and reverse dippers (or risers; SBP-NDR, >1.0).[2] The outcomes were total fatal or nonfatal cardiovascular events (CVEs), which for most of the studies were a composite of acute myocardial infarctions and strokes plus cardiovascular deaths; coronary heart disease (CHD) events (fatal or nonfatal acute myocardial infarctions and sudden deaths); strokes; total all-cause mortality; and cardiovascular mortality. We regarded total CVEs as the primary outcome of interest because of their comprehensive nature and large numbers, which led to more stable results.

An expanded Methods section is available in the online-only Data Supplement where details on the inclusion criteria into the meta-analysis, on the ABPM methods of each cohort, and on the specific ad hoc data analyses performed by each lead investigator were provided.

Statistical Analysis

All meta-analyses were based on the Knapp–Hartung model and executed by Comprehensive Meta-Analysis software, Version 3.200089, March 24, 2014, and by R version 3.2.2 (R Foundation for Statistical Computing, Vienna, Austria). A 2-tailed probability value of <0.05 was regarded statistically significant. Separate analyses were performed with and without simultaneous adjustment for 24-hour SBP. When considering the joint effects of 24-h SBP and SBP-NDR, we assessed collinearity by inspecting the changes in the Cox model coefficients and SEs of 24-h SBP caused by the addition of SBP-NDR and vice versa. Heterogeneity of hazard ratios (HRs) across cohorts was assessed by the Cochran Q test for heterogeneity, the τ^2 statistic, and the I^2 statistic (which takes values between 0% and 100% and values of 0% to 33%, 34% to 67%, and 68% to 100% suggesting low, intermediate, and high heterogeneity).[23] Significant heterogeneity among cohorts was further explored by random effects metaregression using cohort-level characteristic as potential effect modifiers. Model fit was assessed using the proportion of the between-study variances explained by the covariates (R^2), along with significance tests for each covariate and for residual heterogeneity. In sensitivity analysis, we examined the effect of withdrawing each cohort and analyzing the remaining cohorts to ascertain whether any particular cohort had a major effect on the overall results. Funnel plots and 4 tests were used to evaluate the possibility of small study effects: Orwin Fail Safe N, Egger test, Begg test, and Duval and Tweedie trim and fill method.

Results

Ten cohorts with 17 312 hypertensive patients were included in the ABC-H meta-analysis. Tables S1 to S5 in the online-only Data Supplement outline the main characteristics of each study, including details on comorbidities, adjusted covariables, several features of ABPM measurements, the percentage of patients for whom SBP was taken while being treated, and the definitions of total CVEs. The mean age ranged from 50 to 70 years, proportion of men from 29% to 78%, and mean/median follow-up from 4 to 8 years. Average 24-hour SBP varied from 131 to 140 mm Hg and SBP-NDR from 0.88 to 0.93. The proportion of normal dippers varied from 27% to 54%, extreme dippers from 4% to 20%, reduced dippers from 32% to 46%, and reverse dippers from 5% to 19%. There were 1769 total CVEs, 916 CHD events, 698 strokes, 903 all-cause deaths, and 450 cardiovascular deaths. Data quality was moderate-to-high, as previously reported.[22]

Tables 1 and 2 present the main effects (summary HRs) and heterogeneity analyses of nocturnal SBP fall parameters for each end point, with and without simultaneous adjustment for 24-hour SBP, and the forest plots of the analyses for total CVEs are shown in Figures 1 and 2. The SBP-NDR, with or without adjustment for 24-hour SBP, predicted all end points (borderline for strokes), with summary HRs varying from 1.12 (for CHD events and strokes) to 1.23 (for cardiovascular mortality) for a 1-SD increment in SBP-NDR. In simultaneously adjusted analyses, summary HRs of 24-hour SBP were all significant and higher than those of SBP-NDR, varying from 1.26 (for all-cause mortality) to 1.51 (for cardiovascular mortality), for a 1-SD increment in 24-hour SBP. There was no evidence of major collinearity between SBP-NDR and 24-h SBP because their HRs and SEs were virtually unchanged regardless of the order in which these indices were included into the models.

The nondipping pattern, after adjustment for 24-hour SBP, also predicted all end points, except CHD events, with an excess risk ranging from 33% for all-cause mortality to 57% for cardiovascular mortality, in contrast to dipping patients. About dipping subgroups, the reverse dippers had increased risks for all end points with summary HRs varying from 1.57 (for CHD events) to 1.89 (for strokes), after simultaneous adjustment for 24-hour SBP. Otherwise, the reduced dippers had a significant 27% higher risk for total CVEs but nonsignificant excess risks for the other outcomes in contrast to the normal dipper patients.

In overall analysis (Tables 1 and 2), the extreme dipper patients had a nonsignificant increased risk of total CVEs, CHD, and stroke events but a nonsignificant lower risk of all-cause and cardiovascular mortalities than normal dippers; however, their heterogeneity was high, particularly for total CVEs. To clarify the source of this heterogeneity, we tested trial characteristics using metaregression (Table S6) and found that whether the cohort was treated or nontreated for hypertension at baseline was statistically significant in modifying the effect of extreme dipping (P<0.001; after adjustment for multiple testing). Moreover, the inclusion of treatment status into the metaregression model reduced the I^2 from 63% to 0% and increased the P value for

Table 1. Main Effects and Heterogeneity Results of Meta-Analyses of Nocturnal BP Fall Parameters for Prediction of Total Cardiovascular, Coronary, and Cerebrovascular Events, With and Without Adjustments for 24-Hour SBP

		Total Cardiovascular Events		Coronary Events		Strokes	
		Main Effect	Heterogeneity	Main Effect	Heterogeneity	Main Effect	Heterogeneity
Dipping Parameters	Adjustment for 24-h SBP	HR (95% CI)	τ, I^2	HR (95% CI)	τ, I^2	HR (95% CI)	τ, I^2
SBP-NDR (1-SD increment)	Without 24-h SBP	1.20 (1.13–1.28)*	0.037, 20%	1.16 (1.06–1.26)†	0.054, 21%	1.19 (1.06–1.33)†	0.090, 37%
	With 24-h SBP	1.15 (1.08–1.22)*	0.040, 22%	1.12 (1.03–1.22)‡	0.046, 16%	1.12 (0.99–1.25)	0.100, 58%‡
24-h SBP (1-SD increment)	With SBP-NDR	1.39 (1.27–1.51)*	0.075, 45%	1.27 (1.16–1.40)*	0.051, 17%	1.49 (1.35–1.65)*	0.058, 17%
Nondipping (vs dipping)	Without 24-h SBP	1.50 (1.30–1.74)*	0.080, 16%	1.24 (1.01–1.54)‡	0.106, 15%	1.53 (1.23–1.91)†	0.070, 6%
	With 24-h SBP	1.40 (1.20–1.63)†	0.069, 12%	1.20 (0.94–1.53)	0.164, 29%	1.43 (1.15–1.77)†	<0.001, 0%
Subgroups of dipping (vs normal dippers)							
Extreme dippers	Without 24-h SBP	1.16 (0.76–1.77)	0.436, 60%†	1.20 (0.83–1.72)	0.010, 4%	1.42 (0.83–2.42)	0.462, 47%
	With 24-h SBP	1.20 (0.77–1.87)	0.471, 63%†	1.24 (0.86–1.78)	0.107, 4%	1.43 (0.85–2.41)	0.448, 46%
Reduced dippers	Without 24-h SBP	1.37 (1.15–1.64)†	0.142, 35%	1.17 (0.94–1.46	0.120, 16%	1.40 (0.99–1.97)	0.344, 55%‡
	With 24-h SBP	1.27 (1.06–1.53)‡	0.157, 39%	1.10 (0.86–1.41)	0.168, 29%	1.28 (0.90–1.82)	0.361, 57%‡
Reverse dippers	Without 24-h SBP	2.00 (1.64–2.44)*	0.118, 18%	1.70 (1.32–2.20)†	<0.001, 0%	2.15 (1.50–3.09)*	0.273, 33%
	With 24-h SBP	1.79 (1.43–2.22)*	0.154, 26%	1.57 (1.21–2.03)†	<0.001, 0%	1.89 (1.26–2.82)†	0.331, 41%

BP indicates blood pressure; CI, confidence interval; HR, hazard ratio; NDR, night-to-day ratio; and SBP, systolic blood pressure.
*P<0.001.
†P<0.01.
‡P<0.05.

heterogeneity from 0.004 to 0.79; all variability among cohorts was explained by the metaregression model. Furthermore, among cohorts treated for hypertension at baseline, extreme dipping relative to normal dipping carried a borderline reduced risk (summary HR, 0.72; 95% confidence interval, 0.52–1.00; P=0.050), whereas among cohorts of untreated patients, extreme dipping was hazardous (HR, 1.92; 95% confidence interval, 1.24–2.96; P=0.006) as can be seen in Figure 3.

In sensitivity analyses withdrawing 1 cohort at a time, there was no particular cohort that significantly influenced the main results (Figure S1). There was little evidence for small-study effects based on inspecting the funnel plots (Figure S2). Likewise, the 4 different statistical tests for small-study effects provided no evidence for this phenomenon (Table S7) although the power to detect this problem may have been limited by the number of included studies.

Table 2. Main Effects and Heterogeneity Results of Meta-Analyses of Nocturnal BP Fall Parameters for Prediction of All-Cause and Cardiovascular Mortalities, With and Without Adjustments for 24-Hour SBP

		All-Cause Mortality		Cardiovascular Mortality	
		Main Effect	Heterogeneity	Main Effect	Heterogeneity
Dipping Parameters	Adjustment for 24-h SBP	HR (95% CI)	τ, I^2	HR (95% CI)	τ, I^2
SBP-NDR (1-SD increment)	Without 24-h SBP	1.18 (1.06–1.32)*	0.074, 35%	1.31 (1.14–1.50)*	0.100, 33%
	With 24-h SBP	1.13 (1.03–1.24)‡	0.052, 20%	1.23 (1.08–1.40)*	0.082, 25%
24-h SBP (1-SD increment)	With SBP-NDR	1.26 (1.15–1.39)†	0.052, 18%	1.51 (1.37–1.68)†	<0.001, 0%
Nondipping (vs dipping)	Without 24-h SBP	1.40 (1.13–1.73)*	<0.001, 0%	1.72 (1.24–2.40)*	0.142, 11%
	With 24-h SBP	1.33 (1.07–1.65)‡	<0.001, 0%	1.57 (1.15–2.15)‡	0.066, 2%
Subgroups of dipping (vs normal dippers)					
Extreme dippers	Without 24-h SBP	0.72 (0.47–1.12)	0.154, 8%	0.68 (0.35–1.34)	<0.001, 0%
	With 24-h SBP	0.76 (0.47–1.24)	0.224, 15%	0.71 (0.36–1.41)	<0.001, 0%
Reduced dippers	Without 24-h SBP	1.17 (0.96–1.42)	0.096, 5%	1.40 (1.00–1.96)	0.205, 23%
	With 24-h SBP	1.17 (0.90–1.53)	0.202, 40%	1.28 (0.89–1.84)	0.232, 27%
Reverse dippers	Without 24-h SBP	1.88 (1.07–3.31)‡	0.443, 65%*	2.15 (1.24–3.73)‡	0.420, 47%
	With 24-h SBP	1.73 (1.01–2.95)‡	0.408, 60%‡	1.84 (1.08–3.15)‡	0.382, 41%

BP indicates blood pressure; CI, confidence interval; HR, hazard ratio; NDR, night-to-day ratio; and SBP, systolic blood pressure.
*P<0.01.
†P<0.001.
‡P<0.05.

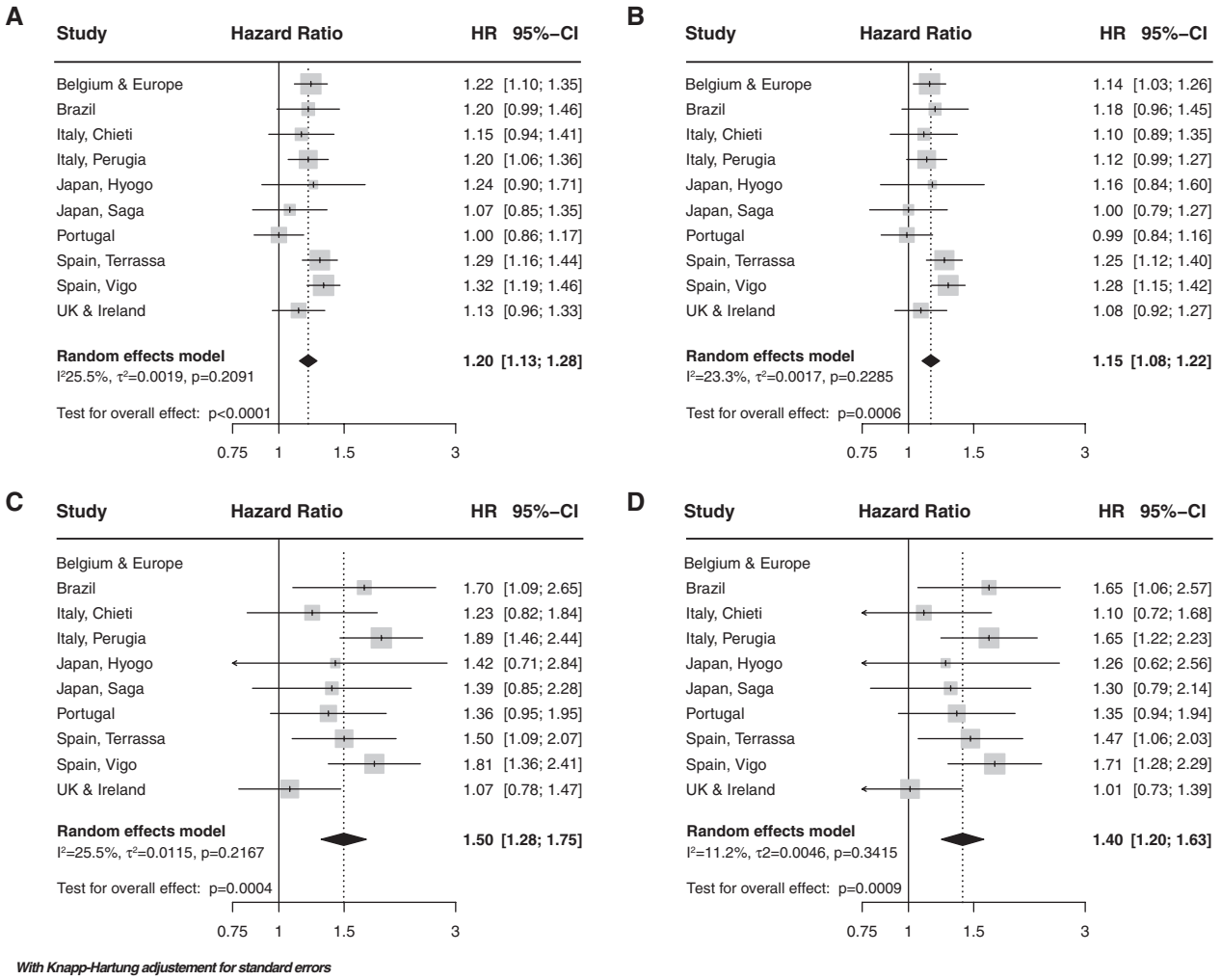

Figure 1. Forest plots of the meta-analysis of the systolic night-to-day ratio (**top**) and the nondipping pattern (**bottom**), without (**A** and **C**) and with (**B** and **D**) simultaneous adjustment for average 24-hour systolic blood pressure, for total cardiovascular event occurrence. CI indicates confidence interval; and HR, hazard ratio.

Discussion

The present meta-analysis of 17 312 hypertensive patients from 3 continents has the following main findings: (1) the nocturnal BP decline, examined as the continuous systolic NDR and adjusted for average 24-hour SBP, is an independent predictor of all adverse outcomes although its HRs (estimated for comparable 1-SD increments) were lower than those of 24-hour SBP. (2) When examined in the traditional dipping/nondipping classification, the nondipping pattern also predicted all end points, except CHD events, after simultaneous adjustment for 24-hour SBP. (3) When examined as the 4 different dipping subgroups, the reverse dippers (risers) had the worst prognosis for all outcomes and seemed responsible for most of the nondipping pattern adverse prognosis although the reduced dippers still had a significant 27% excess risk for total CVEs in contrast to normal dippers subgroup. (4) The effect of extreme dipping on cardiovascular prognosis was significantly influenced by antihypertensive treatment at baseline: among cohorts with treated patients, extreme dipping carried no increased risk, whereas among untreated cohorts, extreme dipping carried an elevated risk for total CVEs with an HR point estimate of 1.9, a value higher than that for reduced dippers (1.3) and similar to that for reverse dippers (1.8). Overall, these findings confirmed the prognostic importance of a blunted nocturnal BP fall independent of ambulatory 24-hour BP levels and add a new insight into the inconsistent reports on extreme dipping. This meta-analysis is the largest in hypertensive individuals and is unique in that it comprehensively evaluated all aspects of the circadian BP variability profile.

There were at least 2 previous meta-analyses in hypertensive patients assessing the prognostic value of nocturnal BP fall parameters.[4,9,10] These previous articles were critical in identifying the hypotheses examined in this study and were state-of-the-art at the time that they were executed. The first one,[9,10] with 3468 individual patients' data, reported that the NDR predicted only all-cause mortality and that the reduced dippers had no increased cardiovascular risk.[10] The second meta-analysis,[4] with 3325 to 4686 hypertensive patients, reported, on the contrary, that the systolic NDR was predictive of total CVEs but not of mortality. However, an analysis of dipping subgroups was not performed.[4] The present ABC-H meta-analysis, with a 4- to 5-fold greater number of patients, consolidated these findings and resolved the controversies

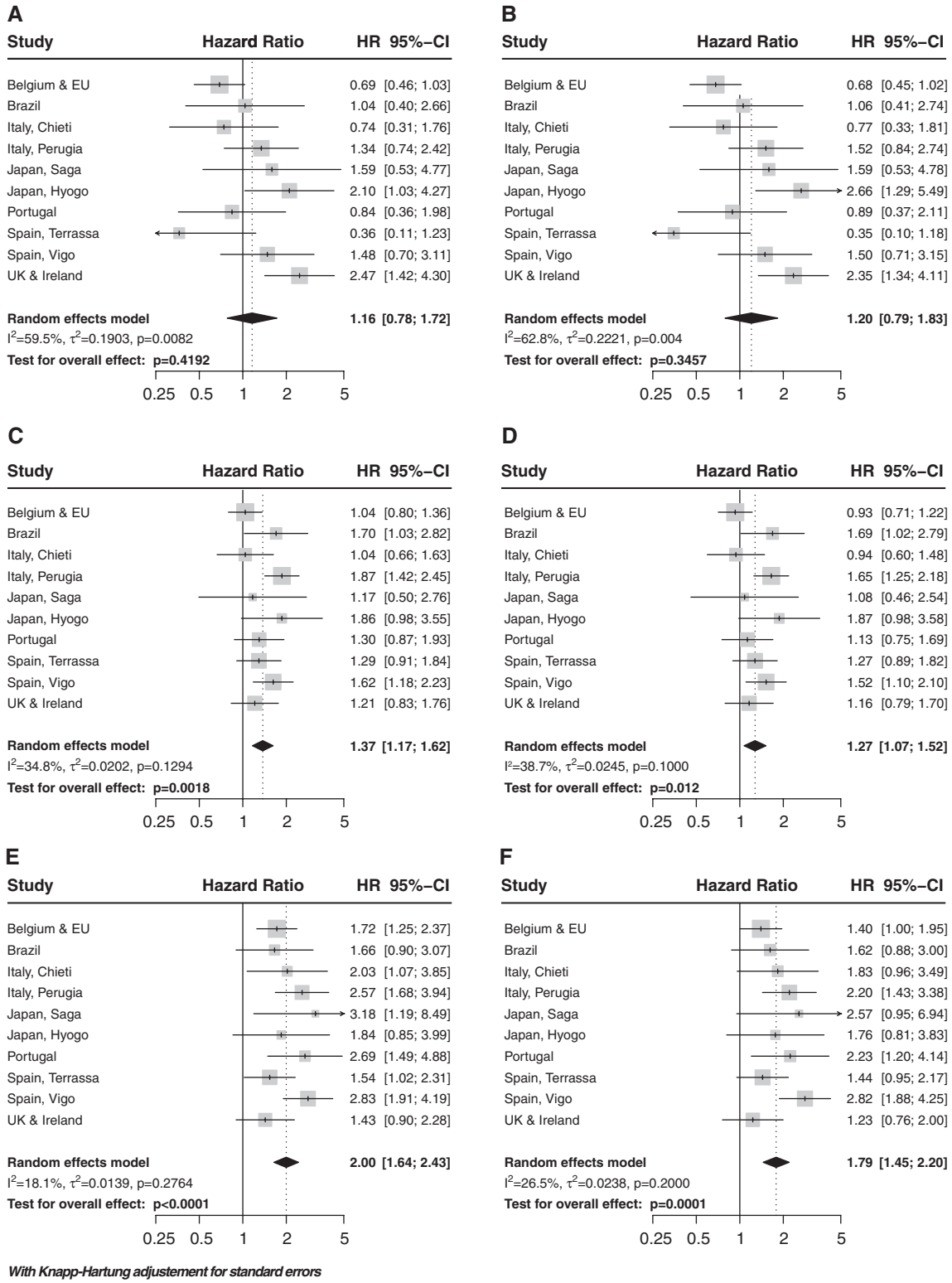

Figure 2. Forest plots of the meta-analysis of the extreme dipping pattern (**top**), the reduced dipping pattern (**middle**), and the reverse dipping pattern (**bottom**), without (**A**, **C**, and **E**) and with (**B**, **D**, and **F**) simultaneous adjustment for average 24-hour systolic blood pressure, for total cardiovascular event occurrence. CI indicates confidence interval; and HR, hazard ratio.

pertaining to these issues. In particular, we demonstrated that the reduced dipper subgroup still had a significant excess risk of total CVE occurrence in contrast to normal dippers. Hence, this specific nocturnal BP fall pattern may not be considered a benign one in terms of cardiovascular risk.

The prognostic importance of the extreme dipping pattern has been disputed.[24] The Belgian meta-analysis,[10] which included 61% of treated hypertensives, suggested that it might be protective for mortality, whereas a cohort study of elderly untreated Japanese hypertensive individuals[7] reported that it

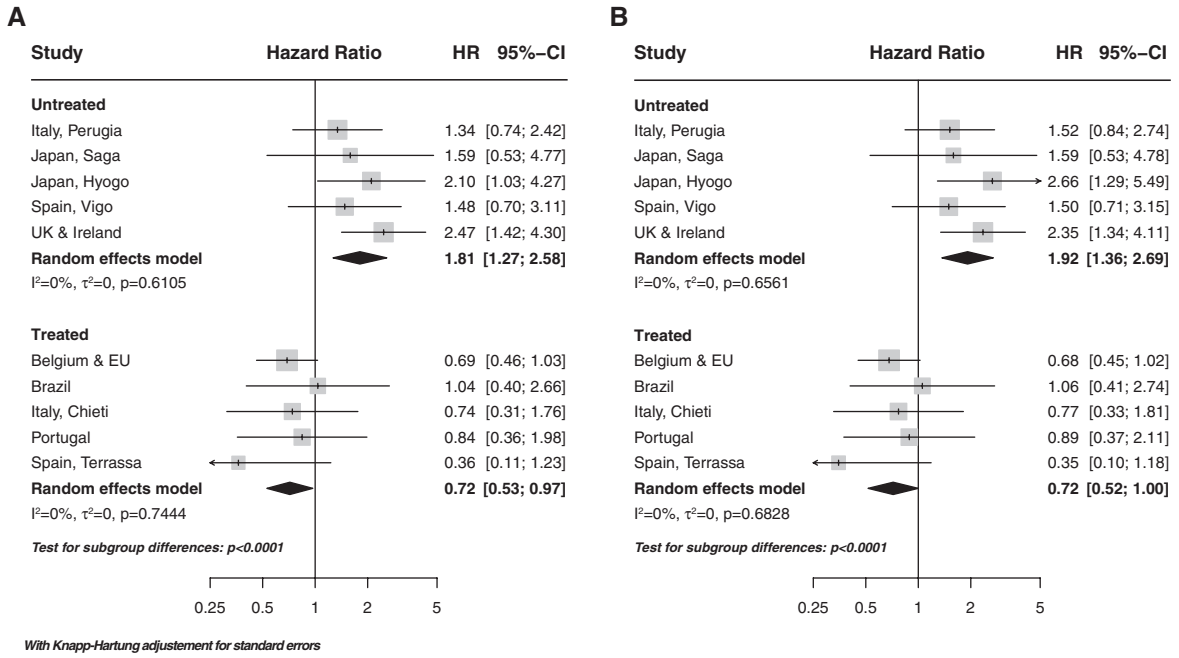

Figure 3. Forest plots of the meta-analysis of the extreme dipping pattern for total cardiovascular event occurrence separated for cohorts that included treated and only untreated hypertensive patients at baseline without (**A**) and with (**B**) adjustment for average 24-hour systolic blood pressure. CI indicates confidence interval; and HR, hazard ratio.

was associated with future ischemic stroke occurrence. About the possible association with stroke occurrence, 3 studies of the ABC-H reported significantly increased risks: the Perugia study[8,17] (HR, 2.54), the Hyogo study[7] (HR, 2.59), and the United Kingdom and Ireland study[12] (HR, 2.70), all of them with untreated patients at baseline. The other studies reported nonsignificant increased or decreased risks (with HRs between 0.58 and 1.46). The summary main effect was a nonsignificant 43% excess risk, with moderate heterogeneity among studies. Total CVE end point followed the same pattern of strokes but with higher heterogeneity, which was almost completely explained by antihypertensive treatment status during ABPM performance. Therefore, the best evidence from the largest meta-analysis is that the cardiovascular risk associated with the extreme dipping pattern seemed significantly influenced by antihypertensive treatment status at baseline: in untreated patients, it may be deleterious, with HRs comparable with those of the reverse dippers, whereas in treated patients, it seemed to carry no additional risk or even might be protective. Nevertheless, these treatment-related findings came from a cohort-level metaregression analysis and should be viewed as hypothesis generating. Rather than treatment effects, other factors may be causing the observed heterogeneity from extreme dipping, such as those related to different populations or geographic areas (the so-called ecological bias of cohort-level metaregressions). Thus, this hypothesis must be tested in individual-level data.

The physiopathologic mechanisms underlying the association between a blunted nocturnal BP fall and a worse cardiovascular prognosis, although extensively discussed,[25] remain largely unproved. Speculations include nocturnal autonomic imbalance favoring sympathetic overactivity,[26] altered baroreceptor sensitivity,[26,27] increased liability of myocardial repolarization,[27] increased salt sensitivity or renal dysfunction, with nocturnal volume overload needing higher nighttime BPs to sustain natriuresis,[21,28] the presence of sleep-disordered breathing conditions or poor sleep quality,[8,29] hyperaldosteronism status,[30] increased arterial stiffness,[31] chronic low-grade inflammation and endothelial dysfunction,[32,33] and daytime orthostatic hypotension.[25,34] On the other hand, the physiopathological mechanisms underlying the possible differential prognostic effect of extreme dipping pattern according to antihypertensive status are completely unexplored, but we may speculate that it might involve orthostatic hypertension, exaggerated morning BP surge, increased BP variability, or increased arterial stiffness in extreme dippers,[24,35,36] which may partially be attenuated by antihypertensive treatment.

This meta-analysis has some limitations that warrant discussion. First, it is a cohort-level meta-analysis, in which some additional analyses, such as interactions and improvement in risk prediction, could not be performed. However, these analyses were not central to our principal aim. Second, the metaregression analysis pertaining to extreme dipping may be affected by an undetected confounding factor although exploration of other potential characteristics failed to support this. Also, a confounder would have to be strongly related to both extreme dipping and cardiovascular risk to account for the ≈2-fold increased risk from extreme dipping. Nonetheless, the finding on extreme dipping should be regarded as hypothesis generating. Third, there were some important differences across cohorts in baseline ABPM methods, particularly on the criterion to define daytime/nighttime periods (fixed periods versus individual diaries/actigraphy), which might have influenced our results although for most of the analyses heterogeneity among studies was only low to moderate. Fourth, some potential important covariates were lacking, such as the sleep quality during ABPM performance. It has been demonstrated that a poor sleep quality during ABPM may not only

falsely increase the nondipping prevalence[37,38] but also abolish its prognostic significance.[8] Also, changes in antihypertensive treatment during follow-up, which might have influenced changes in the nocturnal BP fall, were not available. Finally, the question of the poor reproducibility of nondipping pattern cannot be overemphasized.[38,39] Except for the study from Vigo, Spain,[16] where a 48-hour ABPM was performed, possibly allowing a greater accuracy in nondipping diagnosis, the other studies performed only one 24-hour ABPM examination at study entry. Otherwise, these 2 limitations, lack of sleep quality information and potential low reproducibility of nondipping patterns, would tend to bias data analysis toward the null hypothesis; hence, the prognostic value of a blunted nocturnal BP fall demonstrated here may even be stronger.

Perspectives

The ABC-H meta-analysis, the largest with hypertensive patients, demonstrated that a blunted nocturnal BP decline and the extreme dipping in untreated hypertensives were predictors of worse outcomes, independent of average ambulatory 24-hour BP levels. One previous study suggested that a normal dipping pattern can at least partially be restored by bedtime antihypertensive drug administration[40] and that an achieved lower nighttime BP may yield significant cardiovascular protection.[41] These results highlight the urgent need for studies to determine whether restoration of normal dipping patterns will be capable of reducing cardiovascular events and mortality.

Disclosures

None.

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Novelty and Significance

What Is New?

- This study is much larger (17 312 hypertensive patients) and more diverse (10 populations from 3 continents) in comparison with previous meta-analyses. Therefore, we were able to marshal much greater statistical power for an overall effect and examine many populations for heterogeneity.

What Is Relevant?

- This study provides ambulatory blood pressure monitoring indices for predicting cardiovascular morbidity and mortality. These results can be used to identify patients at risk.
- This study supports that randomized trials must be conducted to determine whether correction of aberrant nocturnal BP fall patterns will lead to reductions in cardiovascular events and total mortality.

Summary

The Ambulatory Blood Pressure Collaboration in Patients With Hypertension (ABC-H) meta-analysis, the largest and most diverse in hypertensive patients, demonstrated that a blunted nocturnal systolic blood pressure fall, both assessed as the continuous night-to-day ratio and as categorical nondipping subgroups, was a predictor of all adverse outcomes, independent of ambulatory average 24-hour systolic blood pressure levels. The prognostic importance of the extreme dipping pattern seemed to be significantly influenced by antihypertensive treatment status, being hazardous only in untreated hypertensive patients.