COMMENTS AND RESPONSES

Response to Comment on: Hermida et al. Influence of Time of Day of Blood Pressure–Lowering Treatment on Cardiovascular Risk in Hypertensive Patients With Type 2 Diabetes. Diabetes Care 2011;34: 1270–1276

We thank Rossen and Hansen (1) for their interest in our article (2). The participants represented a consecutive series of patients fulfilling the exclusion/inclusion criteria who were recruited from those referred to the hospital for evaluation by ambulatory blood pressure monitoring (ABPM) mainly to confirm or reject the diagnosis of hypertension inferred by clinic cuff blood pressure measurement. Diagnosis of hypertension in our trial was based on accepted ABPM criteria, i.e., an awake systolic blood pressure (SBP)/diastolic blood pressure (DBP) mean ≥135/85 mmHg and/or an asleep SBP/DBP mean ≥120/70 mmHg (3). Despite a recommended target goal for clinic SBP/DBP in diabetes of 130/80 mmHg, current guidelines do not provide separate ABPM threshold values for patients with and without diabetes (3). Patients with diabetes in our trial can be considered newly diagnosed hypertensive because a previous ABPM evaluation was not available for any participant before recruitment.

Patients were randomly assigned to one of two monotherapy treatment time groups, either upon awakening (control group) or at bedtime (experimental group). Assignment of participants to treatment time groups was done according to the order of recruitment, following allocation tables constructed for each allowed medication by a computerized random number generator. If patients were uncontrolled based on ABPM criteria after 3 months of therapy, additional medications could be added in keeping with current clinical practice. Additional medications were not randomized according to treatment time. At the final evaluation, the percentages of patients in the experimental group ingesting 1, 2, or ≥3 medications at bedtime were 56.5, 25.0, and 18.5%, respectively. As previously stated (2), the sample size of our trial is limited to derive conclusions from the comparison between classes of medications and their combinations on the benefits, in terms of cardiovascular risk reduction, of bedtime treatment. Extensive reviews on the morning/evening treatment time differences in asleep blood pressure regulation of different classes of hypertension medications are already available (4).

CIs for event rates can be directly calculated from the numbers of events and participants, plus the median duration of follow-up. As stated (2), the rate of total events was significantly higher in the control (54.2 [95% CI 43.4–65.1]) than in the experimental group (19.8 [12.1–27.4]; $P < 0.001$). The rate of major events was also significantly higher in the control group (17.6 [10.6–24.5] vs. 5.2 [1.1–9.2]; $P < 0.001$) (2).

With respect to the results described in Fig. 2 of our article (2), hypertension treatment, and not just the severity of disease, markedly influenced achieved blood pressure. As such, our statements and conclusions on the different shape of the relationship with cardiovascular risk for achieved clinic blood pressure and asleep blood pressure mean seem adequate (2). Data from the baseline ABPM evaluation indicated that cardiovascular risk increased exponentially with progressively increasing asleep blood pressure mean. Baseline clinic blood pressure was not a significant predictor of outcome in the survival model including the asleep blood pressure mean as a confounding variable (5). Finally, analyses of changes in blood pressure during follow-up revealed a significant reduction in cardiovascular risk associated with the decrease in asleep blood pressure mean during follow-up, independently of changes in clinic or awake blood pressure mean (2,5).

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No potential conflicts of interest relevant to this article were reported.

References

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