**ROLE OF TIME-OF-DAY OF HYPERTENSION TREATMENT ON THE**

**J-SHAPED RELATIONSHIP BETWEEN BLOOD PRESSURE AND CARDIOVASCULAR RISK**

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Objectives: It has been suggested that the relationship between treatment-induced blood pressure (BP) reduction and cardiovascular (CVD) outcomes is J-shaped, decreasing as BP is lowered and rising again as BP is decreased further. We investigated the role of hypertension treatment-time on the relationship between treatment-achieved clinic and ambulatory BP and CVD risk.

Methods: We prospectively studied 2156 hypertensives (1044 men/1112 women), 55.6+/-13.6 years of age, randomized to ingest all their hypertension medications upon awakening or at least one of them at bedtime. BP was measured for 48h at baseline, and again annually or more frequently (quarterly) after adjustments in treatment.

Results: After a median follow-up of 5.6 years, a J-shaped relationship was detected between total CVD events and clinic as well as awake BP mean, but only for the group of patients ingesting all medications upon awakening. In patients who ingested medications at bedtime, CVD risk progressively diminished in a linear, rather than J-shaped, manner with treatment-induced decrease in the awake BP mean. The adjusted hazard ratio of CVD events was significantly lower with the progressive reduction in the asleep BP mean, independent of hypertension treatment-time.

Conclusions: Bedtime hypertension treatment is not associated with a J-shaped relationship between BP and CVD risk. The decreased CVD risk associated with the progressive reduction in the asleep BP, more feasible by bedtime than morning hypertension treatment, indicates the need to consider the timing of hypertension medications in conjunction with ABPM as an improved means of reducing CVD risk of hypertensive patients.