The aim of the present study was to assess the relative role of repeated clinic blood pressure (BP) measurement, mean 24 h BP, and diurnal BP rhythm in predicting the development of sustained hypertension in subjects with borderline to mild hypertension.

We studied prospectively 1062 (771 males), never treated, stage 1 hypertensive subjects from the multicenter HARVEST study. All subjects underwent 24 h ambulatory monitoring at baseline and repeated clinic BP measurement during the first six months of follow-up. Patients were classified as nondippers, dippers, or extreme dippers according to whether their night-time systolic BP fall was <10%, 10-20%, or >20% daytime values, respectively. The independent prediction of clinic BP, of 24 h BP and of the non-dipper condition for outcome was tested in a multivariable Cox analysis controlling for possible confounders.

During a mean (95% CI) follow-up of 68 (65-71) months, 236 subjects developed sustained hypertension (clinic diastolic BP permanently > 99 mmHg) and were started on antihypertensive treatment. At baseline, 329 subjects were classified as nondippers, 617 as dippers, and 116 as extreme dippers. The three groups were balanced for sex distribution, and had similar age (33±9, 33±8, and 32±8 years, respectively; n.s.) and baseline clinic BP (145±10/94±6, 146±11/94±6, and 146±11/94±5 mmHg, respectively; n.s.). Night-time systolic BP fall was 7±6, 20±4 and 32±5 mmHg, respectively, in the three groups. When only baseline data were used, mean 24 h BP was the strongest predictor of outcome (p<0.0001), followed by clinic BP (p=0.002), and nondipping status (p=0.026). When all clinic BP measurements taken during the first 6 months of follow-up were taken into account, a great increase in the predictive power of clinic BP was seen (p<0.0001). However, both mean 24h BP (p=0.0001) and nondipping status (p=0.01) were still predictive of outcome. In the subjects stratified by dipping status, the highest rate of end-points was found among the nondippers and the lowest rate among the extreme dippers.

In conclusion, these results obtained in a population of never treated borderline to mild hypertensives indicate that blunted BP fall at night yields prognostic information over and above that provided by clinic BP and mean 24h BP. At variance with the results obtained by other authors in elderly hypertensive individuals, the extreme-dipper condition is not associated with worse outcome in young subjects in the early phase of the disease.

Key Words: Borderline Hypertension, Ambulatory Blood Pressure, Non-dippers

OR-59
PREDICTORS OF SUSTAINED HYPERTENSION IN SUBJECTS WITH BORDERLINE TO MILD HYPERTENSION. A 5-YEAR FOLLOW-UP OF THE HARVEST STUDY
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In older subjects a higher pulse pressure estimated by 24 h ambulatory monitoring was a better predictor of outcome. A 5-year follow-up of the HARVEST study showed that in older subjects a higher pulse pressure derived from conventional blood pressure readings is associated with worse prognosis. We investigated in older subjects whether their night-time systolic BP fall was <10%, 10-20%, or >20% daytime values, respectively. The independent prediction of clinic BP, of 24 h BP and of the non-dipper condition for outcome was tested in a multivariable Cox analysis controlling for possible confounders.

During a mean (95% CI) follow-up of 68 (65-71) months, 236 subjects developed sustained hypertension (clinic diastolic BP permanently > 99 mmHg) and were started on antihypertensive treatment. At baseline, 329 subjects were classified as nondippers, 617 as dippers, and 116 as extreme dippers. The three groups were balanced for sex distribution, and had similar age (33±9, 33±8, and 32±8 years, respectively; n.s.) and baseline clinic BP (145±10/94±6, 146±11/94±6, and 146±11/94±5 mmHg, respectively; n.s.). Night-time systolic BP fall was 7±6, 20±4 and 32±5 mmHg, respectively, in the three groups. When only baseline data were used, mean 24 h BP was the strongest predictor of outcome (p<0.0001), followed by clinic BP (p=0.002), and nondipping status (p=0.026). When all clinic BP measurements taken during the first 6 months of follow-up were taken into account, a great increase in the predictive power of clinic BP was seen (p<0.0001). However, both mean 24h BP (p=0.0001) and nondipping status (p=0.01) were still predictive of outcome. In the subjects stratified by dipping status, the highest rate of end-points was found among the nondippers and the lowest rate among the extreme dippers.

In conclusion, these results obtained in a population of never treated borderline to mild hypertensives indicate that blunted BP fall at night yields prognostic information over and above that provided by clinic BP and mean 24h BP. At variance with the results obtained by other authors in elderly hypertensive individuals, the extreme-dipper condition is not associated with worse outcome in young subjects in the early phase of the disease.

Key Words: Borderline Hypertension, Ambulatory Blood Pressure, Non-dippers

OR-60
AMBULATORY PULSE PRESSURE AS PREDICTOR OF OUTCOME IN OLDER PATIENTS WITH SYSTOLIC HYPERTENSION

In older subjects a higher pulse pressure derived from conventional blood pressure readings is associated with worse prognosis. We investigated whether ambulatory measurement of pulse pressure and mean pressure can refine risk stratification.

808 older (≥60 years) patients with systolic hypertension (160-219/≤95 mm Hg) were randomized to nitrendipine (10-40 mg/day) with the possible addition of enalapril (5-20 mg/day) and/or hydrochlorothiazide (12.5-25 mg/day) or to matching placebos. At baseline, pulse pressure and mean pressure were determined from six conventional blood pressure readings and from 24 h ambulatory recordings. With adjustment for significant covariables, we computed mutually adjusted relative hazard rates associated with 10 mm Hg increases in pulse pressure or mean pressure. In the placebo group, the 24 h and nighttime pulse pressures consistently predicted total and cardiovascular mortality, all cardiovascular events, stroke, and cardiac events. Daytime pulse pressure predicted cardiovascular mortality, all cardiovascular endpoints, and stroke. The hazard rates for 10 mm Hg increases in pulse pressure ranged from 1.25 to 1.68.

Conventionally measured pulse pressure predicted only cardiovascular mortality with a hazard rate of 1.35. In the active-treatment group compared with the placebo patients, the relation between outcome and ambulatory pulse pressure was attenuated to a non-significant level. Mean pressure determined from ambulatory or conventional blood pressure measurements was not associated with poorer prognosis.

In older patients with isolated systolic hypertension higher pulse pressure estimated by 24 h ambulatory monitoring was a better predictor of adverse outcomes than conventional pulse pressure, probably because it reflects more accurately the dynamic interaction between heart and large arteries. In contrast, conventional and ambulatory mean pressures were not correlated with a worse outcome.

Key Words: Cardiovascular Diseases, Hypertension, Mortality

OR-61
CIRCULATING BLOOD PRESSURE PATTERNS IN NORMAL PREGNANCY, GESTATIONAL HYPERTENSION, AND PREECLAMPSIA
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Changes in circadian variation of blood pressure (BP) could be used either to predict preeclampsia or to assess its severity. We have examined and compared characteristics of circadian variability in BP in healthy and complicated pregnant women who were systematically monitored throughout gestation. We analyzed 2430 BP series sampled by ambulatory monitoring for 48 consecutive hours once every 4 weeks from the first obstetric visit until delivery in 235 women with uncomplicated pregnancies, 128 with gestational hypertension, and 40 with a final diagnosis of preeclampsia. The circadian pattern of BP variation for each group and trimester of gestation was established by population multiple-components analysis [Fernandez & Hermida. Chronobiol Int. 1998;15:191-204]. The differences in 24-hour mean and amplitude between healthy and complicated pregnancies were highly significant in all trimesters (always P<0.001). Results further indicated similar circadian characteristics between gestational hypertension and preeclampsia in the first trimester of pregnancy. The difference between these two groups in circadian mean was statistically significant for systolic (P=0.002) but not for diastolic BP (P=0.076) in the second trimester, and for both variables in the third trimester (P<0.001). The differences in BP between healthy and complicated pregnancies, that can be observed as early as in the first trimester of pregnancy, are found when both systolic and diastolic BP for women with a later diagnosis of gestational hypertension or preeclampsia are well within the accepted range of normotension. These differing changes in the circadian pattern of BP with advancing gestational age between healthy and complicated pregnancies offer new end points that may lead to an early identification of hypertensive complications in pregnancy as well as to the establishment of prophylactic intervention.
Patients with elevated blood pressure (BP) during sleep (nondipper BP profile) have excess hypertensive target organ damage and appear to be at increased risk for cardiovascular complications. However, the nondipper BP profile has modest reproducibility on repeat studies with as many as 30-40% of subjects changing categories. In order for nocturnal BP to be a therapeutic target, a better method of assessing nocturnal BP is needed. In both clinical and research terms, it may be more appropriate to characterize ambulatory BP profiles by absolute rather than proportional reductions in BP during sleep. We therefore compared 3 definitions of nocturnal BP in 129 placebo treated patients who had duplicate ambulatory BP recordings 4-8 weeks apart. The patients were 77% male, 53% Caucasian, with an average age of 52 years. The average nocturnal BP was 139/85 mmHg (range, 107-184/64-110 mmHg). The definitions and reproducibility parameters are shown in the Table.

The definitions of a nondipping BP profile based on either a <10% or <5% decline in nighttime BP relative to the daytime BP were less reproducible than using a limit of >125/80 mmHg. Reproducibility was better for systolic than diastolic BP. These data support using an absolute value of BP to define nocturnal BP, especially in clinical trials, rather than proportional reductions from daytime BP values.

### Definitions of Nocturnal BP

<table>
<thead>
<tr>
<th>BP Type</th>
<th>Statistical test</th>
<th>&lt;10% drop</th>
<th>&lt;5% drop</th>
<th>Nocturnal BP*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic</td>
<td>% remaining nondippers</td>
<td>66.1</td>
<td>47.8</td>
<td>91.0</td>
</tr>
<tr>
<td></td>
<td>Kappa statistic</td>
<td>0.38</td>
<td>0.31</td>
<td>0.49</td>
</tr>
<tr>
<td>Diastolic</td>
<td>% remaining nondippers</td>
<td>54.0</td>
<td>40.0</td>
<td>78.0</td>
</tr>
<tr>
<td></td>
<td>Kappa statistic</td>
<td>0.38</td>
<td>0.29</td>
<td>0.46</td>
</tr>
</tbody>
</table>

* American Society of Hypertension recommendation.

Key Words: Dippers/Nondippers, Nocturnal Hypertension, Ambulatory Blood Pressure