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COMMENTARY

We need more evidence for antihypertensive treatment guided by home blood pressure

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Numerous studies of cardiovascular outcome trials have demonstrated the benefit of antihypertensive treatments based on the measurement of office or clinic blood pressure (OBP). However, several observational studies and meta-analyses have clearly demonstrated that out-of-office BP is superior to OBP for the diagnosis and prediction of future cardiovascular morbidity and mortality.[1–6] Two methods of out-of-office BP measurement have been widely investigated: 24 h ambulatory blood pressure monitoring (ABPM) and home blood pressure (HBP) monitoring. However, these methods exhibit apparent differences. HBP monitoring is performed only in a sitting posture, but ABPM is performed during various daily activities, including exercise, working and sleep. HBP is more convenient, available and less expensive than ABPM.[7] However, these methods should be used differently for the assessment of BP characteristics in clinical settings. HBP is convenient for daily use, and it can evaluate daily changes in blood pressure. By contrast, ABPM is superior for the detection of white-coat hypertension and masked hypertension, which may not be detected when BP measurement times are fixed. The British National Institute for Health and Clinical Excellence guidelines for the management of hypertension recently recommended that all patients with elevated OBP should include ABPM to confirm the hypertension diagnosis.[8] HBP is an alternative method to confirm hypertension diagnoses in patients who cannot tolerate ABPM.[8] The British guidelines recommend using these methods to exclude unnecessary treatments for white-coat hypertension. However, the Japanese guidelines seek to establish HBP as the primary tool for evaluating BP status.[9]

Cardiovascular outcome trials using HBP have been delayed compared with ABPM, but evidence of the utility of HBP has accumulated in the past two decades. Most hypertension guidelines, including the Japanese guidelines, recommend HBP for the better management of hypertension.[8–11]

CARDIOVASCULAR OUTCOME STUDIES BASED ON HBP IN OBSERVATIONAL COHORTS

Most cardiovascular outcome studies using HBP have been performed primarily in observational cohorts of the general population.[1–4,6] There are numerous differences between these studies, including the study population, methods of HBP measurements, primary outcomes, the methods of HBP evaluation and statistical adjustments.[1,2,7,10] HBP is superior to OBP for the prediction of future cardiovascular outcomes in most of these studies despite the considerable methodological and clinical heterogeneity.[1–4,6,7,10] Importantly, only a few studies have examined a large number of treated hypertensive patients[5,12,13](Table 1). In one large prospective cohort of 4939 treated hypertensive patients, the baseline OBP and HBP were examined as predictors of cardiovascular outcome.[5] These patients were followed-up for a mean of 3.2 years. Each 10 mm Hg increase in systolic HBP, but not OBP, increased the risk of cardiovascular outcome by 17.2% (95% confidence interval, 11.0–23.8%).[5] This study suggests that HBP is a better predictor of cardiovascular morbidity and mortality than OBP in hypertensive patients and the general population.[5] A recent meta-analysis of the usefulness of HBP for the prediction of cardiovascular morbidity and mortality confirmed that HBP exhibited significant prognostic value even after adjustment for OBP. Conversely, OBP was not significant after adjustment for HBP.[2]

PROGNOSTIC SIGNIFICANCE OF HBP-GUIDED ANTIHYPERTENSIVE TREATMENT

Only two randomized clinical trials have examined the hypothesis that HBP is a better guide for antihypertensive treatment than OBP measurement[14,15](Table 2). The treatment of hypertension based on home or office blood pressure[14] and the home *vs.* office measurement reduction of unnecessary treatment[15] demonstrated that adjustments in antihypertensive treatment based on HBP led to less intensive drug treatment and marginally lowered medical costs, but it also exhibited less long-term BP control. No differences in general well-being and target organ damage were observed.[14,15] However, these two trials had short follow-up periods, which could not support the hypothesis that HPB is superior to OBP. One potential reason that this study did not detect the superiority of HPB is the short follow-up period. No previous trials have assessed long-term cardiovascular outcomes following HBP-guided antihypertensive treatment. Therefore, more long-term prospective outcome trials are required to confirm the prognostic significance of HBP and firmly establish the threshold values for on-treatment HBP.

The report in this issue of *Hypertension Research* by Asayama *et al.*[16] may answer this

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Table 1 Studies of prognostic value of home blood pressure for cardiovascular outcomes

Study, year	*Total,* n	*Subjects*	*Follow-up, years*	*Number of CV events*	*Primary outcome*	*Prognostic values HBP* vs. *OBP*
SHEAF,[5] 2004	4932	treated hypertensive patients	3.2	324	CV death, MI, stroke, TIA angina, CHF, PCI, CABG	HBP > OBP
Ohasama,[12] 2010	2390	general population including treated hypertensive patients	11.9	242	stroke	HBP = OBP
J-HEALTH,[13] 2008	4596	treated hypertensive patients	3.5	60	CV death, MI, stroke	HBP = OBP

Abbreviations: CABG, coronary artery bypass grafting; CHF, congestive heart failure; CV, cardiovascular; HBP, home blood pressure; MI, myocardial infarction; OBP, office blood pressure; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.

Table 2 Studies of usefulness of antihypretensive treatment guided by home blood pressure

Studies, year	*Total,* n	*Subjects*	*Follw-up, years*	*Primary outcomes*
THOP,[14] 2004	400	treated hypertensive patients	1.0	BP levels, intensity of drug Tx, LVM, symptom, costs of Tx
HOMERUS,[15] 2007	430	treated hypertensive patients	1.0	BP levels, intensity of drug Tx, LVM, MAC, symptom, costs of Tx
HOMED-BP,[16] 2012	3518	treated hypertensive patients	5.3	non-fatal MI, non-fatal stroke, CV death

Abbreviations: BP, blood pressure; CV, cardiovascular; HOMED-BP, hypertension objective treatment based on measurement by electrical devices of blood pressure; HOMERUS, home *vs.* office measurement reduction of unnecessary treatment; LVM, left ventricular mass; MAC, urinary microalbumin concentration; MI, myocardial infarction; THOP, treatment of hypertension based on home or office blood pressure; Tx, treatment.

unsolved question. The Hypertension Objective treatment based on Measurement by Electrical Devices of Blood Pressure (HOMED-BP) study is a large intervention trial in Japan with the aim of determining optimal target BP levels on the basis of self-measured HBP and optimizing initial antihypertensive drug treatments. A total of 3518 hypertensive patients were randomized to usual (125–134/80–84 mm Hg) *vs.* tight (<125/<80 mm Hg) control of HBP levels and three initial antihypertensive drug treatments (angiotensin-converting enzyme (ACE) inhibitor, angiotensin II receptor blocker or Ca channel blocker).[16] The primary outcome was a composite of non-fatal stroke, non-fatal myocardial infarction and cardiovascular death[16]. This study also examined the advantages of new technology, which transmits the HBP measurements to the physician over the Internet.[16] The HOMED-BP study was primarily negative regarding the original hypothesis, and the most positive results were observed in sub-analyses or *post-hoc* analyses. However, this study provides useful data for hypertension management. The strengths of this study include the large data set (3518 subjects from 457 general practices throughout Japan, with median follow-up period was 5.3 years); the use of an optimal methodology for HBP monitoring, namely, an Internet-assisted treatment guide; and data collection without observer bias.[16] Asayama *et al.*[16] demonstrated that 25 and 26 primary endpoints were observed in the usual and tight control groups (both 1759 patients), respectively, during the follow-up period. The risk of primary outcomes in a post-hoc analysis of all patients independently increased by 41 and 47% for a 1-s.d. increase in baseline (12.5 mm Hg) and follow-up (13.2 mm Hg) systolic HBP without J- or U-curve phenomena, respectively. The level of the on-treatment systolic HBP measurement that corresponded with a 5-year risk of primary outcome of 1% or less was 131.6 mm Hg. The BP lowering effects and incidences of primary outcome were similar among the Ca channel blocker, ACE inhibitor and angiotensin II receptor blocker groups.[16]

BP increases the risk for cardiovascular diseases in individuals with hypertension and across the full range of BP levels.[17] The established threshold values of on-treatment HBP are not determined. Optimal protection against primary outcome was observed at ~130 mm Hg for systolic HBP in the HOMED-BP study.[16] A total of 68.3% of the patients in the usual control group reached the target systolic HBP of 125–134 mm Hg, and treatment-related adverse effects were very low.[16] Therefore, a systolic HBP of 130 mm Hg is an achievable and safe target.

The present data are useful for the treatment of hypertension in the clinical setting. However, several limitations for this purpose should be noted. First, the cardiovascular event rate of the subjects in the present study was surprisingly low; only 51 primary outcomes occurred in the HOMED-BP study.[16] The low incidence of primary outcomes may be explained by the following factors: the actual risk in this population was low; the BP levels of patients were in stage 1 or stage 2; only 15% of patients had diabetes; and 3% of the patients had previous cardiovascular diseases. Therefore, we cannot extend the present results to high-risk patients. Second, the present study excluded subjects with white-coat hypertension. The difference in systolic BP between HBP and OBP is small (2–3 mm Hg).[16] Therefore, the present study did not provide information on the management of white-coat hypertension. However, HBP and ABPM are particularly useful methods in the treatment of patients with white-coat phenomena. Third, the memory-recording automatic HBP monitors and data collection through the Internet are advanced and useful techniques for the removal of observer bias.[7] The use of memory-recording systems is strictly recommended for patients in clinical trials.[7] However, this system is not widely available in the real world of clinical practice. Self-reports of the HBP values do not always reflect the true values.[18] Therefore, we should be cautious to avoid bias when HBP is used without a memory-recording system in the clinical setting. Clinics and other health care centers should acquire HBP devices with memory-recording systems for the precise evaluation of patient BP status.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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