

White-Coat Hypertension Versus Sustained Hypertension in Japan

To the Editor:

Khattar and associates recently described the extent of target organ damage and the cardiovascular prognosis of white-coat hypertension in a middle-aged adult population.¹ Pickering, who introduced the concept of "white coat hypertension" in clinical practice, provided editorial comments.² The major conclusion of the study was that white-coat hypertension is relatively benign in hypertensive adult patients. There is some debate on the extent of target organ damage in white-coat hypertension. Some reports have concluded that target organ damage is advanced in white-coat hypertension compared with normotension, but others have not found any differences.

There are important difference in the demographics of hypertensive target organ damage. In Japan, coronary artery disease is much less common and cerebrovascular disease more common than in Western countries. In our cross-sectional study using ambulatory blood pressure (BP) monitoring, silent lacunar infarction, a strong predictor of clinically overt stroke, was detected by brain MRI in 26% of elderly subjects with white-coat hypertension (mean [95% CI] age 72 [69–74] years; 34% male), whereas it was found in 52% of subjects with sustained hypertension.³ Thus, we believe that the benefits of antihypertensive treatment in Japanese to prevent stroke would be low in white-coat hypertension. We appreciate the comment of Dr Pickering that the use of ambulatory BP monitoring to distinguish white-coat hypertension from sustained hypertension is clinically important.

In addition, the prognosis of white-coat hypertension would be determined by coexisting target organ damage, especially in an older population. Recently, we identified 236 white-coat hypertensives by a cutoff value for ambulatory BP of 130/80 mm Hg (mean [SD] age 71 [12] years; 34% male) in 821 older hypertensive Japanese patients. In the follow-up period of 43 (14 months [mean (SD)]), 5 had a clinically overt stroke (3 cerebral infarction and 2 cerebral hemorrhage). Left ventricular hypertrophy was found in 60% (3 patients) of those who had a stroke, whereas it was detected only in 5.2% (12) of the remaining 231 subjects with white-coat hypertension. In addition, in 5 white-coat hypertensives who had a stroke, silent lacunar infarction had been detected by brain MRI before the event in all 4 subjects, and 3 of the 4 had multiple infarctions (3 or more lacunae per person). We have previously described patients with white-coat hypertension who developed sustained hypertension that required antihypertensive treatment after the acute major stress of the Hanshin-Awaji earthquake.⁴ Those cases all had target organ damage (microalbuminuria). Thus, in high-risk elderly subjects with white-coat hypertension who already have silent target organ damage, we should pay attention to the possibility that sustained hypertension or cardiovascular morbidity might be triggered by additional stressful events.

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Response

The work of Dr Kario and his colleagues provides further support for the clinical utility of the concept of white-coat hypertension. In a very different population from the one studied by Khattar et al,¹ and with very different outcomes, it was previously observed that elderly Japanese with white-coat hypertension have a low prevalence of cerebrovascular ischemic lesions compared with patients with sustained hypertension² and, as described in the letter, a relatively benign prognosis. The coexistence of target organ damage in patients with white-coat hypertension is certainly important. They are not a homogeneous group, and several reports have shown that target organ damage does occur in some patients with white-coat hypertension, although less frequently than in sustained hypertension. Dr Kario's results suggest that the subgroup of patients with both white-coat hypertension and target organ damage are at increased risk and hence should be treated. However, for everyday clinical practice, some measures of target organ damage, such as brain MRI, are impractical, while others, such as microalbuminuria, are cheap and simple to perform. Recent work has demonstrated the prognostic significance of microalbuminuria,³ and a strong case can be made for its wider use.

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Response

The prognostic implications of white-coat hypertension have remained an area of debate for many years, and we thank Kario and colleagues for their comments regarding our findings. Much of the controversy regarding outcome has been fueled by conflicting reports from cross-sectional studies comparing the extent of target organ damage in white-coat hypertension versus normotension and sustained hypertension. Whereas some studies have reported white-coat hypertension to be associated with adverse cardiac, renal, peripheral vascular, and metabolic alterations, other researchers have failed to detect any end-organ abnormalities in this condition. The relative extent to which these contradictory findings can be attributed to differences in the applied definitions of white-coat hypertension, demographic characteristics, and methodological divergences is difficult to ascertain. Nevertheless, without exception, currently available longitudinal studies have shown significantly lower cardiovas-

cular event rates in white-coat hypertensives than in sustained hypertensives, on a population basis. Therefore, in comparative terms, white-coat hypertension appears to be more benign than sustained hypertension for any given length of follow-up. However, on an individual basis, we readily accept that the presence of target organ damage in a patient with white-coat hypertension may confer an adverse outcome for that particular individual. The presence of left ventricular hypertrophy is an established predictor of coronary and cerebrovascular events, independent of blood pressure level. Moreover, an independent relationship between left ventricular hypertrophy and carotid atherosclerosis has been demonstrated in previously untreated hypertensives,¹ consistent with the data of Kario et al showing an increased prevalence of left ventricular hypertrophy in the group of white-coat hypertensives who experienced a stroke. This might suggest that mechanisms unrelated to blood pressure may be responsible for the target organ damage observed in white-coat hypertension and that antihypertensive treatment under these circumstances may not be appropriate. Indeed, in our study, the event rate in white-coat hypertensives was 9.7% over a 10-year period,² which in accordance with current guidelines does not merit specific blood pressure-lowering strategies.³ Nevertheless, a recent small longitudinal study showed that $\approx 75\%$ of patients designated as having white-coat hypertension on baseline ambulatory blood pressure monitoring developed sustained hyperten-

sion on repeat testing, after a 5- to 6-year follow-up period.⁴ Although larger studies are required to substantiate this finding, careful long-term surveillance of patients with white-coat hypertension, even those without target organ damage, would be prudent to detect the potential development of sustained hypertension and the need for specific antihypertensive therapy.

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