Relentless Progression Toward Sustained Hypertension

Franz H. Messerli, Harikrishna Makani

Blood pressure (BP) measured carefully by cuff under standardized conditions in physician offices has been shown to be an acceptable predictor of morbidity and mortality. However, 24-hour ambulatory BP monitoring is a closer surrogate end point for heart attack and stroke than office BP. Because the correlation between 24-hour ambulatory BP measurement and office BP measurement is moderate at best, not unexpectedly there will be a significant number of people who are truly hypertensive but in whom the diagnosis is missed by office BP measurements (masked hypertension). Conversely, BP may be elevated in the office but not on ambulatory BP monitoring, an entity known to most clinicians as white-coat hypertension.

Both masked hypertension and white-coat hypertension can be considered prehypertensive states not uncommonly evolving into sustained hypertension. The article by Mancia et al in the present issue of Hypertension assesses the risk of developing sustained hypertension in the Pressioni Arteriose Monitorate e Loro Associazioni population over a 10-year follow-up. Regardless of whether the definition of white-coat hypertension or masked hypertension was based on home BP measurements or 24-hour ambulatory monitoring, both forms of hypertension were at an increased risk of progressing to sustained hypertension. In fact, Mancia et al showed that >40% of patients having white-coat or masked hypertension will develop sustained hypertension over a 10-year period (Figure). In contrast, only 16% of truly normotensive subjects will progress to sustained hypertension within the same time span. Of note, both true normotensives and true hypertensive patients had the highest odds of remaining in the same category.

When compared with normotensives, white-coat hypertensives had a 2.5-fold increased risk and masked hypertension a 1.8-fold increased risk of developing sustained hypertension. These results clearly indicate that neither of the 2 conditions should be shrugged off as innocent observations. Both white-coat hypertension and masked hypertension need to be identified and diagnosed and deserve to be monitored carefully. Not only is their risk in evolving into sustained hypertension substantial, but they have been shown to convey, by themselves, an elevated risk of heart attack, stroke, and death compared with the normotensive population. Masked hypertension seems to carry a distinctly more serious prognosis than does white-coat hypertension. For the purpose of this editorial, we prepared a meta-analysis assessing cardiovascular events in 11 studies in a total study population of 25 280 subjects, comparing white-coat hypertension, masked hypertension, and true hypertension with truly normotensive subjects. When compared with true normotensives, the hazard rate for white-coat hypertension was 1.170 (95% CI: 0.982 to 1.390), for masked hypertension it was 1.780 (95% CI: 1.550 to 2.050), and for true hypertension it was 1.930 (95% CI: 1.730 to 2.150). This analysis was done with the Review Manager Software from Cochrane, and we used a fixed-variance model, because heterogeneity among the studies was insignificant.

Similar event rates in masked hypertension were reported by Bobrie et al and Pickering et al. Not surprisingly, in the same Pressioni Arteriose Monitorate e Loro Associazioni population, patients with masked hypertension (and those with white-coat hypertension) had a prevalence of echocardiographic left ventricular hypertrophy that was greater than that of normotensive subjects. Also, Liu et al reported the average left ventricular mass index and the prevalence of carotid plaque as similar in patients with masked hypertension compared with those with sustained hypertension. Inappropriate target organ disease (ie, inappropriate for office BP levels), therefore, should trigger suspicion of masked hypertension and motivate physicians to expose a susceptible patient to 24-hour ambulatory BP monitoring.

Of note, the news is not all bad when looking at the study of Mancia et al. A substantial number of patients regressed toward normotension or at least toward a hypertensive state that confers a lower morbidity and mortality than sustained hypertension. Almost a quarter of the patients regressed from true hypertension to white-coat hypertension and from masked hypertension to true normotension, and 18% regressed from white-coat hypertension to true normotension. The study by Mancia et al does not give us any clues allowing us to discover patients who are prone to progress or regress in this 10-year time span. Clearly, however, identifying such clues should become a seminal issue, particularly if regression toward normotension or lack thereof would be amenable to intervention.

From a practical standpoint, we should remember that it is much easier to suspect the diagnosis of white-coat hypertension, because patients will usually state that their BP is normal at home. In fact, patients use documented normal home BPs often as an argument for refusing to take additional antihypertensive medication. In contrast, masked hypertension needs to be looked for, and there are very few clinical hints as to its presence. A normal BP in the clinical setting does not mean that a patient is not at risk from an elevated...
BP, which can occur at other times of the day. This is particularly true in patients who are treated with antihypertensive drugs that do not encompass a full 24-hour period. Because most patients take their medication in the morning, BP values in the physician’s office often are normal but may be substantially elevated at the end of the dosing interval (ie, during the night and early morning hours). Thus, in many hypertensive patients, clinic BP is seemingly well controlled, but early morning BP, before the patients take the medication, may be elevated, thereby accelerating the risk of cardiovascular events.9 For both patient and physician, masked hypertension may become a blind spot10 in the antihypertensive regimen. Pickering et al9 have suggested that, for the detection of masked hypertension, home BP monitoring is likely to prove more cost-effective than ambulatory monitoring. As to the therapeutic approach, we should remember that white-coat hypertension has a benign prognosis and may often be over-treated; therefore, a conservative approach is probably justified. Conversely, masked hypertension has a more serious prognosis and is often undertreated; it deserves, therefore, a thorough evaluation and a more aggressive therapeutic approach.

In conclusion, Mancia et al4 have shown that, over a 10-year period, many patients relentlessly marched toward a more severe category of hypertension. However, for unknown reasons, some patients are able to shake the spell and to remain in the same BP category or are even able to go back to a category that confers a lesser morbidity and mortality. Our next challenge will be to identify clinical clues helping to predict in which direction our patients are prone to march.

**Disclosures**

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**References**


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