Editorial Commentary

Masked Hypertension

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The addition of ambulatory blood pressure monitoring to conventional clinic measurement for defining blood pressure status in clinical practice has added a new complexity to the process, because the separation of normotension and hypertension can be assessed independently by each of the 2 methods. We thus have 4 potential groups of patients who are, first, normotensive by both methods (true normotensives); second, hypertensive by both (true, or sustained, hypertensives); third, hypertensive by clinic measurement and normotensive by ambulatory measurement (white-coat hypertensives); and, fourth, normotensive by clinic measurement and hypertensive by ambulatory measurement. From a clinical point of view, the first 2 groups are easy to deal with, because both methods give the same classification. Of more interest are the groups in which there is disagreement. The third group, usually referred to as white-coat hypertensives, or less frequently, as isolated office hypertensives, have been extensively studied and are generally accepted as being at relatively low risk of cardiovascular morbidity, a view consistent with the concept that ambulatory pressure gives a better prediction of risk than clinic pressure.

Until now, little attention has been given to the fourth group, whose condition has been given the awkward titles of “reverse white-coat hypertension” or “white-coat normotension.” If it is true that the ambulatory pressure gives the better classification of risk, it would imply that these people should be regarded as being genuinely hypertensive, as argued below. We also propose that the phenomenon might be called “masked hypertension,” on the grounds that the hypertension is not detected by the routine methods. “Undetected ambulatory hypertension” is another possible title. But what evidence is there that this group deserves recognition as a discrete entity, as opposed to being made up of people who happened to have an unusually high ambulatory pressure or a low clinic pressure on that particular occasion? There are potentially several questions that could be asked to decide this issue. First, the phenomenon of masked hypertension would be more credible if it could be shown that it is reproducible on repeat testing. As far as we are aware, this issue has not been examined. Second, patients with masked hypertension should show more extensive target organ damage than true normotensive subjects. Here we are on surer ground. The first study to look at this issue was our publication of 1999, in which we showed that the masked hypertensive group had left ventricular mass and carotid atherosclerosis that were greater than that of true normotensive subjects and that were similar to true hypertensive subjects. The left ventricular mass index was 73 g/m² in the true normotensive subjects, 86 g/m² in the masked hypertensive subjects, and 90 g/m² in the true hypertensive subjects. Carotid plaque was present in 15% of true normotensives and in 28% of both the masked and true hypertensives. More recently, an analysis of the PAMELA data, a population study of 3200 Italians, classified the subjects in the 4 groups that we have described above. Individuals with treated hypertension were excluded from this analysis; 67% were true normotensives, 12% true hypertensives, 12% white-coat hypertensives, and 9% masked hypertensives. The average clinic pressure in the masked hypertensives was 129/84 mm Hg, which, although still within the normal range, was higher than the true normotensives (112/77 mm Hg). The left ventricular mass index was higher in the masked hypertensives (91.2 g/m²) than in the true normotensives (79.4 g/m²) and similar to the true hypertensives (94.2 g/m²). A third issue is whether masked hypertensives are at increased risk of cardiovascular morbidity. This remains to be determined.

What factors might lead to masked hypertension? In principle, there are 2 groups of factors, which are not mutually exclusive. First, the clinic pressure could be relatively low in relation to the ambulatory pressure, or second, there could be factors that selectively raise the ambulatory pressure. With regard to the first possibility, it is generally true that the daytime ambulatory pressure is higher than the clinic pressure in truly normotensive subjects, but in hypertensives the clinic pressure tends to be higher. One reason for this is “regression to the mean,” because hypertension status is almost always based on clinic pressure. Many factors could selectively elevate the ambulatory pressure. For example, we showed many years ago that smokers tend to have high daytime ambulatory pressures (when they are likely to be smoking) in comparison with their clinic pressures (when they are not likely to be smoking). Second, subjects who are more physically active during the day will tend to have higher daytime pressures.

Several population studies have compared clinic and ambulatory blood pressures. Some have shown daytime pressures to be a little higher than clinic pressures, whereas others have found the reverse. One important finding from an Italian population study has been that the ambulatory pressure shows much less increase with age than the clinic pressure.
In a Danish study, 86% of men 42 years of age had daytime pressures higher than the clinic pressure, whereas this was true of only 51% at the age of 72 years. The white-coat effect (the difference between the clinic and ambulatory pressure) is hence more marked in older people, and because masked hypertension is equivalent to a negative white-coat effect, it is reasonable to suppose that masked hypertension would be less prevalent with increasing age.

A major issue concerns the prevalence of masked hypertension. Although there are no definitive data, the available information is disturbing. In a study of 319 clinically normotensive volunteers, all of whom had 5 clinic measurements and 12-hour daytime ambulatory blood pressure measurements, Selenta et al found that 23% had masked hypertension, defined as a daytime blood pressure >135/85 mm Hg. Subjects with masked hypertension tended to be male, past smokers, and older, and they had consumed more alcohol. The issue of masked hypertension was also discussed by Belkic et al, who referred to it as occult workplace hypertension. We found that 36 of 267 men (13.5%) in the Cornell Worksite study had masked hypertension, defined as a daytime ambulatory diastolic pressure >85 mm Hg and a clinic pressure <85 mm Hg. Two population-based studies have also described the phenomenon. The first was the Ohasama study conducted in a small Japanese town, which reported that 10.2% of subjects with normal screening blood pressures had ambulatory pressures that were in the “borderline hypertensive” range (>133/78 mm Hg for 24-hour average) and another 3.2% in the definitely hypertensive range (24-hour blood pressure >144/85 mm Hg). The second was the PAMELA study quoted above, which found it in 9% of subjects. But even if the prevalence was only 5%, this number applies to the whole adult population, not just the population of hypertensives, so in the case of the United States, this might amount to 10 million people.

It seems clear that masked hypertension should be taken seriously and is a phenomenon worthy of further investigation. If it is accepted that ambulatory blood pressure gives a better prognosis than clinic blood pressure and that the correlation between the two is only moderate, it is logical to propose that there will be a significant number of people who are truly hypertensive but in whom the diagnosis is missed by clinic measurement. But how frequently this phenomenon occurs, and how such individuals should be identified, remains a mystery. Clearly, we cannot argue for screening of the general population, but there are many patients who are referred for suspected hypertension who have normal clinic pressures on repeat testing. Individuals in whom the level of suspicion might be heightened would include those who have a family history of hypertension or other risk factors such as central obesity. Perhaps some of them would benefit from ambulatory monitoring to rule out masked hypertension. Although treatment recommendations may be premature, the finding of masked hypertension in a patient with early signs of target organ damage might act as an incentive to promoting lifestyle changes.

References