High Prevalence of White-Coat Hypertension in Spanish Resistant Hypertensive Patients

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Resistant hypertension is a major public health challenge both in the United States and worldwide. Although various authors use different definitions, a recent scientific statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research defined resistant hypertension as blood pressure either controlled by ≥4 antihypertensive medications or ≥140/90 mm Hg, despite 3 antihypertensive medications of different classes, at near-maximal US Food and Drug Administration-approved doses, one of which is a diuretic. Some authors add a minimum duration of 3 months of such treatment; others insist that the medications must be “appropriately chosen,” the patient adherent, and/or the patient referred by a physician to a hypertension center. Patients with resistant hypertension are of great public health importance, because they have a higher risk of future cardiovascular and renal events, greater healthcare expenditures, a higher prevalence of secondary hypertension and target organ damage, and are, by definition, “difficult to control.” Most reports of the prevalence of resistant hypertension come from tertiary referral centers or from clinical trials that implemented a stepwise sequence of medications to control blood pressure. A major confounder in the office diagnosis of resistant hypertension is the “white-coat effect,” defined as a persistently increased blood pressure in the medical office compared with home (or better) 24-hour ambulatory blood pressure monitoring (ABPM). In the United States, the distinction between the white-coat effect and white-coat hypertension is important, because one criterion for the latter diagnosis (which is required for reimbursement of 24-hour ABPM) is the lack of target organ damage. The procedure is currently not covered for Medicare beneficiaries who have target organ damage, even if their 24-hour ambulatory blood pressure monitor shows an unequivocal white-coat effect. The exact prevalence of the white-coat effect varies, but the usual range in large studies is 18% to 33% across the general hypertensive population. Both white-coat phenomena (effect and hypertension) would be expected to be more common in resistant hypertension than in the general hypertensive population, because neither typically responds well to antihypertensive drug therapy.

In this issue of Hypertension, de la Sierra et al present interesting analyses of data from their large registry of Spanish patients who had 24-hour ABPM performed and were recruited from primary care and specialty clinics since 2004. They carefully gathered data from >68 000 hypertensive patients and determined that 12.2% had resistant hypertension. More interestingly, 37.5% of these 8295 patients had relatively normal 24-hour ambulatory blood pressures, so their elevated clinic pressures could be explained by the white-coat effect, and the remaining 62.5% had “true resistant hypertension.” With the exception of younger age, the latter group had a higher prevalence of each and every cardiovascular risk factor that was examined compared with those who displayed the white-coat effect. In addition, the latter group was more likely to display the “early morning surge” in blood pressure, which has been associated (at least in epidemiological studies) with an increased risk of stroke (49%), acute myocardial infarction (39%), and cardiovascular death (29%).

These data are important because of the large number of included patients, the difficulties involved in gathering similar nationwide data from both primary care and specialty sites (particularly in the United States), and the validation of previous knowledge about the increased risk factor burden and disturbed circadian blood pressure variation in true resistant hypertensives (drawn from much smaller populations, many with inherent selection biases). The authors’ estimate of the prevalence of resistant hypertension is much lower than that garnered from the American Society of Hypertension Registry Initiative, which has a growing database of 265 000 unique hypertensive patients, primarily from North Carolina, South Carolina, Florida, and Georgia (the “Stroke Belt,” where hypertension, uncontrolled hypertension, and its sequelae were once more common than other regions in the United States). Approximately 33% of patients with uncontrolled hypertension in this database were taking ≥3 antihypertensive medications per day. The question thus arises as to whether differences in the prevalence of resistant hypertension could be regional (because of diet, prevalence of hypertension, or access to medical care). It also reinforces other data suggesting that the white-coat effect may be more common in Italy and Spain compared with Northern Europe and North America. Only a very large effort using a standardized protocol would be able to properly address these issues.
The data of de la Sierra et al. also shed some new light on the large group (37% in this report) of patients who would have been classified as “resistant hypertensives” if ABPM had not been performed (as is often the case in the United States). It is still controversial as to how much effect, if any, the white-coat effect has on prognosis and whether such patients should be spared more intensive treatment and investigation. The multivariate analyses of de la Sierra et al. indicate that the risk factor burden of resistant hypertensive patients with the white-coat effect is lower than that of patients without it. However, it is unlikely that the differences in risk factor profile are sufficient to discriminate between these diagnoses; in addition, ABPM is the only way to obtain information about the circadian pattern of blood pressure. These data are consistent with the call from many outside the United States to use ABPM more, for both initial diagnosis and assessment of therapy. One hopes that de la Sierra et al. will enlighten us further in future publications reporting on factors that led to intensification of treatment after ABPM, its results in BP control, and long-term cardiovascular and renal outcomes (and associated healthcare expenditures) in their 2 large cohorts. It is tempting to predict that ABPM might be economically justified, perhaps even in the United States, if future costs for “extra” medications and clinic visits could be avoided, without increasing the risk of very expensive hospitalizations in the group displaying the white-coat effect.

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