White coat hypertension: European versus American guidelines—A new dilemma

Cesare Cuspidi MD1,2 | Federico Paoletti MD1 | Marijana Tadic MD, PhD3

1Department of Medicine and Surgery, University of Milano-Bicocca, Milano, Italy
2Istituto Auxologico Italiano, IRCCS, Milano, Italy
3Department of Cardiology, Charité-University-Medicine Campus Virchow Klinikum, Berlin, Germany

Correspondence: Cesare Cuspidi, MD, Clinical Research Unit, Istituto Auxologico Italiano, IRCCS, Viale della Resistenza 23, 20036 Meda, Italy. Email: cesare.cuspidi@unimib.it

For a long time, since its identification in the early 1980s, white coat hypertension (WCH), alternatively termed “isolated clinic hypertension,” has widely been considered a completely innocent blood pressure (BP) phenotype, that is, a condition for which the normality of BP outside the medical environment, assessed by ambulatory or home BP monitoring, entails a prognostic value similar to normotension.1,2 However, challenging this traditional view, an increasing amount of evidence supports the concept that WCH has an intermediate risk between normotension and sustained hypertension. In a recent meta-analysis of 23 cohorts including 20,445 initially untreated individuals, WCH (defined as high clinic BP but normal out-of-office BP, either by ambulatory or home measurements) was associated with an adjusted 38 and 20% increased risk of cardiovascular disease and total mortality compared with normotension.3

Originally limited to untreated individuals, the definition has more recently been generalized to individuals treated with BP lowering drugs in whom only clinic BP fails to reach the therapeutic target (ie, white coat uncontrolled hypertension [WUCH]).

The association of WUCH with cardiovascular disease and mortality has been reported to be somewhat weaker than that of WCH. Findings from a registry-based, multicenter, national cohort including 63,910 adults showed that WUCH, unlike WCH, exhibited a non-significant increase in full-adjusted risk of cardiovascular (HR 1.04, CI: 0.65-1.66, $P = .86$) and all-cause mortality (HR 1.06, CI: 0.82-1.37, $P = .66$).4 The outcome discrepancy in WCH and WUCH is probably due to the fact that this latter group is more likely to have more frequent medical checks that, in turn, impact favorably on a variety of unhealthy conditions contributing to total cardiovascular risk and, last but not least, benefits from the protective effect of antihypertensive drugs.

Since WCH is quite frequently diagnosed in everyday clinical practice, this condition has important implications for public health. WCH has been estimated to occur in approximately 20%-30% of the general hypertensive population, and its prevalence depends on several individual clinical characteristics (ie, age, gender, office BP, body mass index, and comorbidities) as well as on methods (ambulatory or home BP measurement) and BP cutoffs used to define normal out-of-office values.5

According to the 2018 European Society of Hypertension/European Society of Cardiology (ESH/ESC) guidelines, definition of WCH traditionally relies on elevated office BP (≥140 mm Hg systolic BP and/or ≥90 mm Hg diastolic BP) during repeated visits concomitant with BP values below the accepted thresholds for ambulatory (ie, mean 24-hour systolic BP/diastolic BP <130 and <80 mm Hg) or home hypertension (ie, systolic BP/diastolic BP <135 and <85 mm Hg).6 As for ambulatory BP criteria, due to the clinical and prognostic implications of nocturnal BP, it has been suggested that WCH diagnosis should be preferentially based on mean 24-hour BP, rather than on daytime BP thresholds, thereby incorporating nocturnal BP values in the assessment of this condition. However, it is important to note that in 2017 the American College of Cardiology/American Heart Association (ACC/AHA) hypertension guidelines updated the classification of both office and ambulatory hypertension recommending lower BP thresholds that is 130/80 mm Hg for office and 125/75 mm Hg for 24-hour BP, respectively.7

In view of the differences between the two guidelines, the impact of the new American BP diagnostic criteria compared with traditional ones (ie, confirmed by the ESH/ESC guidelines) on the prevalence of office hypertension has been investigated by some studies that, as expected, found marked increases in the prevalence of both untreated and uncontrolled hypertension.8 On the contrary, the impact of the 2017 ACC/AHA recommendations on the detection of WCH and WUCH in current practice is scanty.

Thus, we have addressed this topic in a large cohort of patients referred to a single outpatient hypertension center to confirm the
diagnosis of office hypertension or evaluate the efficacy of antihypertensive therapy. A total of 7364 individual 24-hour ambulatory BP recordings from untreated individuals and treated hypertensive patients with office systolic BP ≥ 140 mm Hg and/or diastolic BP ≥ 90 mm Hg were analyzed. Based on office and 24-hour ambulatory BP values, subjects were divided into four groups: (a) untreated elevated office systolic or diastolic BP and normal 24-hour ambulatory BP, that is, WCH; (b) untreated elevated office systolic or diastolic BP and elevated 24-hour ambulatory BP, that is, sustained hypertension; (c) treated elevated office systolic or diastolic BP and normal 24-hour ambulatory BP (<130/80 mm Hg), that is, WUCH; and (d) treated elevated office and 24-hour systolic or diastolic BP, that is, uncontrolled hypertension. The prevalence rates WCH and WUCH were assessed according to both European and American hypertension guidelines whose normal 24-hour BP thresholds are <130/80 and 125/75 mm Hg, respectively.

A total of 1284 patients were classified as WCH (17.4%) and 1950 as WUCH (26.5%) according to the 2018 ESC/ESC guidelines; the corresponding numbers, based on the 2017 AHA/ACC guidelines, were 697 (9.4%) and 1156 (15.6%), respectively. These findings strongly suggest that the detection of both WCH and WUCH markedly decreases when applying the AHA/ACC 24-hour BP thresholds and, at the same time, an opposite trend occurs for the sum of sustained untreated and uncontrolled hypertension (from 56% to 75%). However, it should not be ignored that the classification of BP patterns has limited reproducibility over time.

As for WUCH, a recent comprehensive analysis of the European Lacidipine Study on Atherosclerosis showed that its reproducibility was worse than that of patients showing control or lack of control of both office and ambulatory BP. Whether the use of lower 24-hour BP criteria for defining WCH and WUCH can improve cardiovascular risk stratification and preventive strategies in the hypertensive population remains an open question. Data from the Intensive Versus Standard Ambulatory Blood Pressure Lowering to Prevent Functional Decline In the Elderly (INFINITY) study in which intensive treatment of ambulatory BP in older patients was well tolerated and associated with a significant reduction of cardiovascular can be considered an argument in favor of lower ambulatory normality thresholds.

In a practical perspective, the large discrepancy between the two guidelines in detecting BP patterns at different cardiovascular risks (ie, WCH/WUCH versus sustained/uncontrolled hypertension) observed in our registry-based study urgently raises the problem of defining shared diagnostic criteria aimed at optimizing therapeutic strategies worldwide.

CONFLICT OF INTEREST
None.

ORCID
Cesare Cuspidi https://orcid.org/0000-0002-7689-478X
Marijana Tadic https://orcid.org/0000-0002-6235-5152

REFERENCES