Chapter 11
White-Coat Hypertension: Do We Really Understand It Now?

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Introduction

Office blood pressure (BP) is very frequently higher than that measured out of the office. This difference, recognized for more than 70 years [1], has been ascribed to an alert reaction in response to a situation that results unusual for the patient and has been denominated as white-coat effect. White-coat hypertension (WCH), also described as isolated office or isolated clinic hypertension, is a condition in which BP is maintained elevated in iterative visits to the office and is normal when measured on either ambulatory blood pressure monitoring (ABPM) or home blood pressure monitoring (HBPM). Conversely, BP can be normal in the office and be elevated when measured by ABPM or HBPM, this situation is known as masked (MH) or isolated ambulatory hypertension. The recent Guidelines of the European Society of Hypertension/European Society of Cardiology maintain the recommendation that both terms white-coat and masked hypertension should be reserved to qualify untreated individuals [2]. However, both situations are observed frequently in treated hypertensives requiring our attention to adequate the amount of pharmacological therapy in order to ensure the best cardiovascular (CV) and renal protection in these patients.

This chapter reviews in particular the prevalence of WCH, the risk accompanying it, and the clinical attitude during the follow-up of patients presenting with this form of hypertension. These data are confronted with those of masked hypertension in untreated as well as in treated hypertensives. Data obtained from the Spanish ABPM Registry will be used to describe the prevalence of both forms of hypertension in different clinical situations [3]. Particular attention will be paid to WCH and MH in chronic kidney disease (CKD).

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Prevalence of White-Coat Hypertension

Population-based studies reviewed by Fagard and Cornelissen [4] found an overall prevalence of WCH of 13%. This figure increases to 32% in hypertensive subjects. Table 11.1 contains the data of prevalence of WCH obtained in the Spanish ABPM Registry for the general population of treated and untreated hypertensives [5, 6], including the data of men and women [7]. These data have confirmed that WCH is present in a substantial minority of treated and untreated hypertensive patients and that advanced age, female gender, obesity, and a lower prevalence of smokers are the most relevant factors contributing to WCH, confirming previous results [4]. Interestingly, the sensitivity and specificity of the physician in relation to suspect the existence of WCH in untreated hypertensives have been shown to be 52.9 and 59.7%, respectively [6].

The prevalence of masked hypertension was 5.4% in treated hypertensives [5], with lower incidence in females (5.9%) than in males (7.9%, $p < 0.001$) [6]. Data from the Spanish ABPM Registry describe that 38% of untreated hypertensives presenting BP levels within the high–normal range (130–139/85–89 mmHg) in the office are masked hypertensives [3].

Table 11.2 contains the data of the Spanish ABPM Registry reflecting the prevalence of WCH in situations of elevated global CV risk as diabetes [8], coronary heart disease [9], chronic kidney disease (CKD; [10]), and hypertension with high global CV risk [12]. As can be seen, in all these situations accompanied by particularly elevated CV risk, the prevalence of WCH is elevated particularly when office BP is within the high level of prehypertension or within the stage 1 of arterial hypertension. Table 11.2 also contains the percentage of patients initially classified by office BP as having resistant hypertension who present WCH [12]. Even in this situation, WCH is substantially prevalent.

Overevaluation of BP level can also happen in the form of the term "pseudohypertension", used to describe an elevated brachial pressure assessed with a cuff and sphygmomanometer in the context of normal intra-arterial pressure assessed invasively [13]. Messerli et al. [14] indicated that this form of hypertension could be identified on the basis of palpable thickening of the radial artery (Osler positive sign). Ulterior studies have shown that Osler sign has low sensitivity and selectivity

Table 11.1 Prevalence of white-coat hypertension (WCH) in the general population of hypertensives including differences by gender and in untreated hypertensives [2–4]

	(*n*)	%WCH
Treated hypertensives [5]	*12,897*	*21.4*
Male [6]	15,212	24.2
Female [6]	13,936	32.5*
Untreated hypertensives [7]	*6176*	*29.2*[a]

*$p < 0.001$ vs. males

[a] WCH defined as ABP > 135 and/or 85 mmHg during day time. In the remaining it was defined as 24-h ABP > 130 and/or 80 mmHg

Table 11.2 Prevalence of white-coat hypertension (WCH) in treated hypertensive patients with diabetes, coronary artery disease (CAD), chronic kidney disease (CKD), hypertensive at high CV risk (HCVR) divided according to office BP level, and in resistant hypertension [8–12]

	(*n*)	%WCH
Diabetes	*12,600*	*33.0*
CAD	*2434*	*25.2*
CKD	*5693*	*36.8*
HCVR	*4729*[a]	
Office BP		
130–139 and/or 85–89		60.0
140–159 and/or 85–89		42.4
> or = 160/100		23.3
Resistant hypertension	*8295*	*37.5*

[a] Considering as control values of 24-h ABPM < 130 and/or 80 mmHg

[15]. Actually, available evidence suggests that most individuals labeled with the term of "pseudohypertension" have isolated systolic hypertension [13].

Importance of White-Coat Hypertension in Untreated Hypertensives

WCH in untreated hypertensives is important for several reasons [16]: First, the labeling of the patient as being false hypertensive is in itself of some gravity; second, insurability and cost; and third, the skewing of results of clinical trials that could include a significant number of WCH. This would translate into a lower than expected risk in the population studied. In fact, the most recent guidelines from the UK suggest that all new hypertensive patients undergo either ABPM or HBPM [17]. It has been calculated that identification of WCH in England could represent savings in the order of 10.5 million pounds in 5 years [18] based on the fact that identification of WCH provides the opportunity to avoid unnecessary treatment and medical visits.

Organ damage is less prevalent in WCH than in sustained hypertension and prospective studies have consistently shown this to be the case also for CV events and death [4, 19–21]. However, recent data indicate that the white-coat effect is strongly associated with increased arterial stiffness [22, 23], a strong predictor of CV events [2], is associated with carotid atherosclerosis in the general population [24], includes subjects with a widely different long-term risk of a CV event [25], and is accompanied by increased central aortic pressure levels [26]. These data enhance the possibility that in untreated hypertensives, WCH is accompanied by an increased global CV risk and the fact that patients with WCH frequently receive pharmacological therapy could contribute to explain a lower number of CV events [19]. It is also important to note that patients with this condition are prone to develop sustained hypertension over time; it is therefore advisable to monitor these individuals regularly so that antihypertensive therapy can be initiated when appropriate [27].

In contrast to WCH, in untreated people, MH is particularly prevalent in those presenting high–normal BP values in the office. Data from the Spanish ABPM Registry describe that 38% of untreated hypertensives presenting BP levels within the high–normal range (130–139/85–89 mmHg) in the office are masked hypertensives [3].

Importance of White-Coat Hypertension in Treated Hypertensives

As described previously, the prevalence of WCH in treated hypertensives is elevated. The relevance of this finding consists principally on the fact that patients with normal BP levels in ABPM or HBPM do not require further antihypertensive pharmacological therapy because goal BP is already attained. It has been considered that either ABPM or HBPM are required in treated hypertensives in order to have a better idea of the real BP of the patients so as to avoid an inadequate further drop in BP that could provoke unwanted CV and/or renal damage [28, 29]. Nevertheless, data from theHypertension in the Very Elderly Trial (HYVET) have shown positive data for the outcome of elderly hypertensive patients, albeit an estimate of 50% of them presented WCH in the study [30]. The finding of any form of target organ damage in patients with WCH promotes the need to consider pharmacological therapy [2].

The presence of episodic hypertension in treated hypertensives represents an enhanced risk for them [31]. These episodes could be related to the presence of sporadic episodes of WCH and deserve further investigation.

Prevalence and Relevance of Masked Hypertension

As previously commented, the prevalence of MH is high in untreated and treated hypertensives [3]. Several factors contribute to an increase of out-of-office BP such as younger age, male gender, smoking, alcohol consumption, physical activity, anxiety, obesity, diabetes, CKD, family history of hypertension, and office BP values in the high–normal range [32]. The incidence of CV events in untreated MH is similar to that in sustained hypertension [19, 32].

The Relevance of White-Coat Hypertension and Masked Hypertension in Patients with Chronic Kidney Disease

It is well established that CKD is accompanied by a particularly high prevalence of arterial hypertension and also by a very significant increase of CV risk [33]. The most adequate goal BP in CKD has been considered in previous guidelines to be

below 130/80 mmHg or even lower if proteinuria was present [34]. Actually, the goal considered is less than 140/90 mmHg [2] due to the fact that BP control in CKD must contemplate the very frequent simultaneous presence of CV events for which evidences of lower BP goals are absent [35]. In fact, an estimated glomerular filtration rate (eGFR) value below 60 ml/min/1.73 m^2 has to be considered among the five most relevant precipitators for the development of acute coronary syndrome [36] and the same could be said for stroke [37].

The misclassification of BP control at the office is very frequent in hypertensives with CKD. In a recent publication [10] that included 5693 patients with CKD, we observed that 36.8% exhibited WCH and 32.1% presented with adequate control of BP in the office but elevated values out of office. These data point to the need of a more adequate knowledge of the real values of BP control in CKD. Otherwise, over- or undertreatment could contribute to cause an increase in risk in these patients either as a consequence of unnecessary further treatment in WCH or to the development of CV events due to inadequate therapy allowing the persistence of sustained hypertension out of office.

Can the White-Coat Response Be Reduced in the Measurement of Blood Pressure in the Office?

Clinical practice guidelines have traditionally recommended manual BP measurement setting as the standard method for diagnosing hypertension. At present, BP cannot be estimated using a mercury sphygmomanometer in many countries. Auscultatory or oscillometric semiautomatic sphygmomanometers are used instead. These devices should be adequately validated and checked periodically through calibration [2]. The advent of automated office BP (AOBP) represents a new alternative to obtain a more adequate evaluation of BP levels in the office [38]. AOBP consists of obtaining multiple BP readings using a fully automated sphygmomanometer with the patient resting quietly alone. AOBP provides more accurate BP readings and correlates better with ABPM and HBPM values and with the presence of target organ damage [39].

Conclusion

WCH is quite prevalent in daily clinical practice and only using ABPM or HBPM can be adequately detected, albeit AOBP is presenting data that could facilitate an adequate BP estimation in the office. Detection in untreated hypertensives is cost saving (avoidance of treatment and medical visits), albeit the risk of this situation is above that of true normotensives. Follow-up of these patients is required using adequate ways to measure real BP in order to start pharmacological therapy as soon as

they become true hypertensives which happens frequently with time. If target organ damage is detected, pharmacological therapy can be initiated [2].

In treated hypertensives, WCH is also prevalent and it is important to discover its existence to avoid adding unneeded medication. Follow-up with adequate estimation of BP is also required.

On the other hand, the detection of MH requires the initiation of antihypertensive treatment in those previously untreated [2] and probably the reinforcement of treatment in those already receiving antihypertensive drugs.

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