Journal of Hypertension: Open Access

Hänninen, J Hypertens 2014, 3:2
DOI: 10.4172/2167-1095.1000144

Review Article Open Access

Is it Practical to Search for Masked Hypertension?

Marjo-Riitta Hänninen*

Joensuu Occupational Health, Finland

Abstract

Masked hypertension refers to a condition with normal office and elevated home or ambulatory BP without antihypertensive medication. It is a common phenomenon in a general population with a prevalence of 8-17%. However, the persistence of masked hypertension is limited, and agreement between home and ambulatory BP is only moderate. Different definitions for masked hypertension are still used, for example, elevated 24-hour, daytime, working or nighttime BP. Masked hypertension has been associated with high-normal office BP, obesity, male gender, and metabolic or lifestyle risk factors but these findings have not always been consistent. Masked hypertension has also been related to target organ damage, most commonly left ventricular hypertrophy. The cardiovascular risk associated with masked hypertension in a general population is still controversial and may, in part, be related to other concomitant cardiovascular risk factors. There is no evidence on the treatment and cost-effectiveness of masked hypertension. Implementation of out-of-office BP measurement and identification of masked hypertension in clinical practice requires interaction with general practitioners. Further studies need to map and bridge the gaps between experts´ recommendations and needs of general practitioners.

Keywords: Masked hypertension; Home blood pressure; Ambulatory blood pressure; Hypertension

Introduction

Hypertension is an important public health challenge worldwide. It has been identified as the first cause of death worldwide being responsible for 9.4 million premature deaths. Moreover, it has been ranked third as a cause of disability adjusted life-years deteriorating health related quality of life [1-3]. Hypertension is one of the most frequent reasons for adults to visit a physician´s office [3], and 33% of US adults ≥ 20 years of age have been reported to have hypertension [4]. Hypertension is strongly associated with overall cardiovascular risk. Cardiovascular disease is the foremost cause of preventable deaths globally accounting for 30% of all deaths [4,5]. However, approximately half of the disease burden attributable to office BP develops in individuals with hypertension; the remainder develops in those with BP values in the normal range [2,3].

Masked hypertension, a condition with normal office and elevated out-of-office, is often missed in the office visit. Out-of-office BP measurement is required for its identification but multiple office and out-of-office measurements are usually performed only when increased BP values are observed. Inclusion of masked hypertension in the normotensive control group may underestimate the consequences of high BP and benefits of interventions [3,6]. But what evidence is there that masked hypertension should be searched for in general practice?

Prevalence and Definition of Masked Hypertension

Although the term masked hypertension should not be used when a patient is being treated and thus has already been diagnosed as hypertensive, most studies have included treated hypertensive patients [3,6]. Table 1 presents the proportions of masked and white-coat hypertension in population-based studies using home BP measurement [7-14]. In three studies, home BP measurement schedule differed from that recommended by the current European guidelines. In others, home BP was measured for three or seven days. Two studies used the same device for both office and home BP measurement. In most studies, the prevalence of masked hypertension was 8-11% despite differences in study populations, treatment status and measurement schedule. In contrast to masked hypertension, the prevalence of the opposite phenomenon, white-coat hypertension, varied across studies (4-29%). The higher prevalence of masked hypertension found in two studies may have been related to older age, greater proportion of treated patients and the use of only morning home blood pressure [11,13]. When daytime or 24-hour ambulatory BP has been used to define these conditions in a general population, the prevalences have varied from 9 to 17% for masked hypertension and from 8 to 13% for white-coat hypertension [3].

Reproducibility

Five studies have investigated the persistence of masked hypertension in untreated individuals. One study used home BP [15], three daytime ambulatory BP [16-18] and one both [19]. The number of home measurements ranged from 12 to 24 and that of office measurements from 1 to 6. Viera et al. [19] assessed a short-term (1 week) reproducibility of masked hypertension in 50 untreated borderline hypertensive individuals. The reproducibility of masked hypertension was 69% with home BP and 73% with daytime ambulatory BP. In other studies, the follow-up period ranged from 6 months to 5 years. The prevalence of masked hypertension tended to be higher in the second than in the first session due to a decrease in office BP in repeated visits [3]. Of patients with masked hypertension in the first set of measurements, 59% had masked hypertension in the second set when morning home BP was used [15]. Lower percentages were found when only evening home BP was used to define masked hypertension (24%) [15], or in untreated young individuals (38%) [17]. The majority of the previous studies were subject to selection or small-sample biases [3].

Three studies assessed the persistence of masked hypertension or masked uncontrolled hypertension during multiple measurement sessions. In a study of 1669 white-collar workers [18], office BP was

***Corresponding author:** Marjo-Riitta Hänninen, Joensuu Occupational Health, Penttilänkatu 7-9, 80220 Joensuu, Finland, Tel: 358 40 5837650; E-mail: maahann@utu.fi

Received March 05, 2014; **Accepted** March 27, 2014; **Published** March 29, 2014

Citation: Hänninen MR (2014) Is it Practical to Search for Masked Hypertension? J Hypertens 3: 144. doi:10.4172/2167-1095.1000144

	n (participation rate)	Age (years)	Men (%)	Treated (%)	Blood pressure measurements		Prevalence (%)	
					Office	Home	Masked	White-coat
Didima, Greece (9)	662 (76%)	≥ 18	42	16	three in 2 visits (physician)	two in the morning and evening for 3 days	8	5
Ohasama, Japan (10)	1050 (44%)	≥ 55	32	39	two in 1 visit (physician)	one in the morning and evening for 4 weeks	9	29
Hisayama, Japan (11)	2915 (78%)	≥ 40	44	31	three in 1 visit	three in the morning for 4 weeks	22	7
PAMELA, Italy (25)	2051 (64%)	25-74	51	15	three in 1 visit (physician)	one in the morning and evening for 1 day	10	13
Cacciolati et al, France (13)	1814 (87%)	≥ 75	39	51	three in 1 visit	three in the morning and evening for 3 days	16	13
Marquez et al, Spain (14)	1153 (82%)	≥ 18	49	NA	two in 1 visit (interviewer)	two in the morning and evening for 3 days	9	4
Finn-Home, Finland (7)	1459 (87%)	45-74	47	-	two in 1 visit (nurse)	two in the morning and evening for 7 days	8	15
Hänninen et al, Finland (3)	261 (81%)	35-64	47	12	two in 4 visits (nurse)	two in the morning and evening for 7 days	11	2

Table 1: Prevalence of masked and white-coat hypertension in populations.

measured three times and ambulatory BP during working hours. BP was assessed three times over 5 years. The persistence of masked hypertension was 18.5% across all three measurement periods. In a multicenter randomized trial of 161 treated hypertensive patients [20], office and 1 week home BP was measured seven times during one year. Over 50% of patients had masked uncontrolled BP at least once but only half of them had masked uncontrolled BP for a second time during the trial. Only a very small percentage of patients had masked uncontrolled BP for over 5 visits, and in none of the patients masked hypertension persisted for over 6 visits. The limited repeatability may have reflected the effect of antihypertensive treatment rather than the reproducibility of masked hypertension. Consistent results were obtained in a clinical practice-based study of mostly treated hypertensive patients (n=252) who did not have changes in antihypertensive drug therapy. A total of 36% of patients had masked uncontrolled BP at least once with automated office BP and 57% with manual office BP measurement but only 4-6% exhibited masked uncontrolled BP on three consecutive visits during a 2-year follow-up [21].

Masked hypertensive patients may not be a homogenous group. Up to 50% of these patients may be classified as normotensive in the second measurement session [16]. In a European community based Three-City study [22], 26% of masked hypertensive patients became sustained hypertensive during a follow-up of 1 year. Patients with persistent masked hypertension or who progressed from masked to sustained hypertension have had higher LVMI and baseline BP than normotensives. In treated patients, the reproducibility of masked uncontrolled hypertension (44-62%) has been associated with male gender, habitual alcohol intake, a change in antihypertensive treatment, and the quality of office BP measurements [3]. Different definitions are still used to define masked hypertension, for example, elevated 24-hour, daytime, working, or nighttime ambulatory BP (Table 2) [3,6]. In treated patients, 24% of masked hypertensives may have this condition on the basis of only nocturnal BP [23]. Moreover, the reproducibility of masked nocturnal hypertension has been shown to be better than that of masked daytime hypertension [23]. In one study, masked nocturnal hypertension was associated with increased cardiovascular risk but masked daytime or 24-hour hypertension was not [24]. Masked hypertension can also be determined on the basis of elevated home BP. Duplicate morning and evening measurements on three days (12 readings) have been suggested as the minimum requirement for a reliable definition [4]. In most studies, office BP was measured with a mercury sphygmomanometer that is being replaced with non-mercury-containing devices. When assessed by a technician or a nurse, office BP tends to be lower than when it is measured by a physician [3,6].

	Systolic BP (mmHg)		Diastolic BP (mmHg)
Office BP	<140	and	<90
Home BP	≥ 135	and/or	≥ 85
Ambulatory BP			
Daytime	≥ 135	and/or	≥ 85
Nighttime	≥ 120	and/or	≥ 70
24-hour	≥ 130	and/or	≥ 80

Table 2: Definition of masked hypertension.

Home vs. ambulatory BP

The Italian PAMELA study examined 1637 untreated individuals [25]. Home BP was based on the average of only two readings which was compared with the average 24-h ambulatory BP. The prevalence of masked hypertension was 10 % with home or 24-hour ambulatory BP. Only 45-57% of participants having masked hypertension with 24-hour ambulatory BP had masked hypertension with home BP. A similar percentage (48-59%) was found in a Finnish population (n=261). In other studies, the agreement ranged from 23-30% between 24-hour and home (12 readings) BP to 88% between daytime and home (24 readings) BP [3]. Almost all studies used the same type of device, oscillometric, for both ambulatory and home BP measurement. In most cases with disagreement between home and ambulatory BP monitoring, BP values have been close to the diagnostic thresholds. When a 5 mmHg grey zone for uncertain diagnosis has been applied to the BP thresholds, agreement between home and ambulatory has increased to over 90%. Masked hypertensive patients defined with home or ambulatory blood pressure have had similar characteristics, target organ abnormalities and cardiovascular risk [3,8]. However, two Japanese studies suggested that masked hypertension, defined with elevated night-time or 24-hour ambulatory BP might be associated with higher glucose level or target organ damage than masked hypertension defined with home BP [3]. Guidelines recommend ambulatory BP monitoring in diabetic patients in whom masked night time hypertension may be associated with nephropathy [6].

Identification of Masked Hypertension

It should be noted that most studies have included treated

hypertensive patients and been subject to small sample or selection biases. In addition, characteristics may not be identical in masked hypertensive patients defined with home or ambulatory BP [3]. Not all guidelines outline practices to detect masked hypertension. European Society of hypertension recommend out-of-office BP measurement if a patient has high-normal office BP or normal office BP and high cardiovascular risk [6]. However, over 60% of individuals with high-normal office BP do not have masked hypertension [7]. In addition, among treated patients, over 60% of patients with controlled office BP and high cardiovascular risk did not have masked hypertension [23].

Demographic factors

Proposed risk factors for masked hypertension are listed in Table 3 [3,6]. Masked hypertension has frequently been associated with male gender, central obesity and high-normal office blood pressure [3,6]. Other findings have not always been consistent. Several studies have shown that masked hypertension, as well as white-coat and sustained hypertension is associated with older age [3]. Its frequency has even been 52% in individuals older than 80 years of age [13]. However, masked hypertension has sometimes been associated with younger age when ambulatory BP measurement has been used [3,23]. Mean daytime BP is higher than home BP in younger individuals, while mean home BP is similar or higher than daytime BP in elderly individuals [26]. This may, in part, explain the different results obtained from the association of age and masked hypertension. Only two studies have reported that masked hypertensive patients have a family history of hypertension or premature cardiovascular disease. Most of the previous studies failed to find any significant differs, and one study even found a lower frequency of family history in masked hypertension than in normotension [3].

Lifestyle risk factors

Half of the population-based studies have suggested that masked hypertension is associated with current smoking or current, regular or excessive alcohol drinking [3,7,8,11]. The other half have failed to find any significant differences. Only three of the studies investigated untreated individuals. The partially inconsistent findings may be explained by different definitions used, for example, self-reported current, former, habitual or heavy smoking, or a magnitude or duration of exposure in treated or untreated persons [3]. In treated patients, smoking or drinking may impair response or adherence to antihypertensive medication. [6]

Most of the previous studies have not found any significant differences in self-reported physical activity, regular exercise, or energy expenditure [3]. Five of them investigated a large population-based sample and three used home BP measurement. A hypertension clinic based study reported that masked hypertensive patients exercised more frequently than white-coat or sustained hypertensives [27]. Three studies suggested that masked hypertension could be associated with lower physical activity or exercise capacity than normotension [3,28]. Exaggerated blood pressure response to exercise, a predictor of future hypertension, has been associated with masked hypertension [3]. Uzu et al. [29] suggested that high dietary sodium intake might be associated with masked uncontrolled hypertension. Three other studies did not find any significant differences in urinary sodium excretion or estimated sodium intake [3].

Transiently elevated office BP at some time High-normal office BP Younger age Male sex Target organ damage
Multiple risk factors or high cardiovascular risk profile Diabetes Chronic kidney disease Obstructive sleep apnea Coronary or cerebrovascular disease
Family history of hypertension Unfavorable lifestyle (obesity, smoking, drinking) Stressful conditions Anxiety Physical activity
Exaggerated hypertensive response to exercise Increased reaction to standing

Table 3: Proposed risk factors for masked hypertension by review articles or guidelines [3].

Metabolic risk factors

Metabolic risk factors (frequency of dyslipidemia or fasting glucose or insulin levels) of masked hypertensives have often fallen between those of normotensives and those of sustained hypertensives. In an untreated Finnish population (n=1582), almost 60% masked hypertensive patients had metabolic syndrome when harmonised criteria were used. The prevalence of masked hypertension has been particularly high in diabetic patients, and it has been suggested that the detection rate of masked hypertension may increase with the duration of diabetes [3]. In the Italian PAMELA study (n=1412), masked, white-coat and sustained hypertensive patients were at similar risk of developing new-onset diabetes mellitus [30]. The risk was largely accounted for by the metabolic abnormalities in these conditions.

Psychological factors

Masked hypertension has most commonly been associated with job stress [3]. Masked hypertension has also been related to daily interpersonal conflict, shift work, lower score for type A personality (hard-driving, fast-moving and work-oriented person who frequently become impatient, irritable and annoyed) and higher points on Whiteley-7 (more hypochondriac) [3,7,28]. One study suggested that masked hypertensive patients are less depressive than white-coat or sustained hypertensives whereas in another study, masked hypertension was associated with higher points on BDI (more depressive) [7,27]. Other studies failed to find any significant differences in self- or other deception, hostility, depression, anger, perceived social support, or self-assessed health [3].

Target organ damage

A Danish population study showed that individuals with subclinical organ damage and masked hypertension comprise a high-risk group with a 10-year event rate of 12.4%. Inclusion of subclinical organ damage and/or ambulatory BP to detect masked hypertension increased sensitivity of risk stratification (SCORE) but reduced specificity [31]. Masked hypertension has been associated with echo- or electrocardiographic left ventricular hypertrophy (LVH) that has often been intermediate between that of normotension and that of hypertension [3]. In an untreated Finnish population (n=1459), 19% of white-coat hypertensive, 22% of masked hypertensive and 30% of sustained hypertensive participants had electrocardiographically determined LVH when Sokolow-Lyon or Cornell product criteria were used [7].

Fewer studies have evaluated carotid intima-media thickness (IMT) or pulse wave velocity (PWV) in masked hypertension. In the untreated Finnish population (n=592 for IMT and n=158 for PWV) [32], masked and sustained hypertensive patients had higher age- and sex-adjusted IMT and PWV than normotensives. Only the differences

in PWV remained significant after adjustment for confounders. Two other population studies and studies on untreated individuals have suggested that masked hypertension is associated with higher IMT than normotension or prehypertension even after adjustment for confounding factors [3]. Almost all studies that have investigated albuminuria in masked hypertension have been performed in diabetic patients. In the majority of them, masked hypertension was associated with a higher 24-hour urinary albumin excretion or urinary albumin-creatinine ratio than normotensives [3]. In addition, in the Japanese Ohasama study (n=1365), the risk of chronic kidney disease was higher in masked hypertension (OR 2.56) than in normotension [33].

Pathophysiology of Masked Hypertension

The mechanisms responsible for masked hypertension are largely unknown. Masked hypertension has been associated with increased sympathetic nerve activity, attenuated baroreflex-heart rate control, altered microcirculation, adipocyte-derived hormones, and decreased fibrinolytic activity, endothelial dysfunction, inflammation, or BP variability which may contribute to its increased cardiovascular risk. The circadian profiles of BP and heart rate in masked hypertension have showed the same pattern as in normotensive and hypertensive patients [3].

Hypertension arises from a complex interplay between genetic and lifestyle factors. It has been suggested that 30-50% of the variance of BP readings are attributable to genetic heritability [34-36]. There is, however, no data on the genetics of masked hypertension.

Practical Considerations

The association between masked hypertension and other risk factors is important. BP and tobacco smoking are the leading risk factors for global disease burden. Also the increasing prevalence of obesity and type 2 diabetes mellitus are major health problems. It should, however, be noted that BP, as well as blood glucose, is a continuous, not discrete, variable that exerts a dose-dependent effect on cardiovascular risk [4,5].

Six population studies have investigated the cardiovascular risk associated with masked hypertension [3]. Three used home, one 24-hour and three ambulatory BP to define masked hypertension. Confounder adjusted hazard ratios were significantly increased in only two studies using daytime ambulatory BP. Both studies had limitations. One investigated 578 untreated 70-year old men with no history of cardiovascular disease [37]. The other evaluated only stroke, transient ischemic attack and cardiovascular deaths in a Japanese population [38]. Masked or masked uncontrolled hypertension has been associated with increased cardiovascular risk in meta-analyses, and treated hypertensive or diabetic patients [3,4]. In the Italian PAMELA study (n=1412), 40-47% of masked hypertensive participants became sustained hypertensive over a 10-year interval. Independent contributors of the development of sustained hypertension were not only baseline BP but also, to a lesser extent, metabolic variables and age. The increased risk of sustained hypertension did not just result from a reduced distance to the cut-off values defining sustained hypertension. Masked hypertensive participants also showed a greater increase in both office and out-of-office systolic BP than normotensives [39].

Lifestyle modifications and frequent follow-up visits have been recommended for patients with masked hypertension or high-normal office BP and also contribute to the control of other risk factors. The problem is the limited level of adherence to lifestyle changes and low persistence of masked hypertension over time [3,6]. Some guidelines suggest initiation of antihypertensive drug treatment when a patient has high or very high total cardiovascular risk. No clinical trial has ascertained whether treatment of masked hypertension reduces cardiovascular complications, and there is limited data regarding the use of home or ambulatory BP measurement in antihypertensive treatment adjustment [3,6]. Appropriate treatment of other diseases may also affect BP. For example, CPAP (continuous positive airway pressure) therapy has been found to promote significant reduction in office and ambulatory BP and the frequency of masked hypertension in patients with severe obstructive sleep apnea [3].

The cost-effectiveness of home or ambulatory BP measurement has been investigated in patients with elevated office BP. Cost savings have been based on the detection of white-coat hypertension and subsequent reductions in treatment costs and follow-up visits [3,40]. The diagnosis and treatment of masked hypertension is expected to lead to cost savings through reduction of cardiovascular complications. It may actually increase costs in the short-term [3]. Out-of-office measurement may cause discomfort, anxiety, obsessive behaviour or time costs to the patient [6]. Focusing on masked hypertension may also draw attention away from other patients with normal office BP and high cardiovascular risk. Lifestyle changes can and should be prescribed to the control of other risk factors even without out-of-office BP measurement.

Conclusion

There is still limited evidence on the persistence, significance, treatment and cost-effectiveness of masked hypertension. Implementation of out-of-office BP measurement and identification of masked hypertension in clinical practice requires interaction with general practitioners. Further studies need to map and bridge the gaps between experts´ recommendations and needs of general practitioners.

References

1. Mathers C, Stevens G, Mascarenhas M (2009) Global health risks: mortality and burden of disease attributable to selected major risks, World Health Organization, Geneva, Switzerland.
2. Murray CJ, Ezzati M, Flaxman AD, Lim S, Lozano R, et al. (2012) GBD 2010: design, definitions, and metrics. Lancet 380: 2063-2066.
3. Hänninen MR (2014) Masked hypertension in Finland. An independent cardiovascular risk factor? National Institute for Health and Welfare, Finland.
4. Santulli G (2013) Epidemiology of Cardiovascular Disease in the 21st Century: Updated Numbers and Updated Facts. JCvD 1:1-2.
5. Santulli G (2012) Coronary heart disease risk factors and mortality. JAMA 307: 1137.
6. Mancia G, Fagard R, Narkiewicz K, Redòn J, Zanchetti A, et al (2013) 2013 ESH/ESC Guidelines for the Management of Arterial Hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens 31: 1281-1357.
7. Hänninen MR, Niiranen TJ, Puukka PJ, Mattila AK, Jula AM (2011) Determinants of masked hypertension in the general population: the Finn-Home study. J Hypertens 29: 1880-1888.
8. Hänninen MR, Niiranen TJ, Puukka PJ, Jula AM (2010) Comparison of home and ambulatory blood pressure measurement in the diagnosis of masked hypertension. J Hypertens 28: 709-714.
9. Stergiou GS, Baibas NM, Kalogeropoulos PG (2007) Cardiovascular risk prediction based on home blood pressure measurement: the Didima study. J Hypertens 25: 1590-1596.
10. Hara A, Ohkubo T, Kondo T, Kikuya M, Aono Y, et al. (2009) Detection of silent cerebrovascular lesions in individuals with 'masked' and 'white-coat' hypertension by home blood pressure measurement: the Ohasama study. J Hypertens 27: 1049-1055.

11. Fukuhara M, Arima H, Ninomiya T, Hata J, Hirakawa Y, et al. (2013) White-coat and masked hypertension are associated with carotid atherosclerosis in a general population: the Hisayama study. Stroke 44: 1512-1517.

12. Mancia G, Facchetti R, Bombelli M, Grassi G, Sega R (2006) Long-term risk of mortality associated with selective and combined elevation in office, home, and ambulatory blood pressure. Hypertension 47: 846-853.

13. Cacciolati C, Hanon O, Alpérovitch A, Dufouil C, Tzourio C (2011) Masked hypertension in the elderly: cross-sectional analysis of a population-based sample. Am J Hypertens 24: 674-680.

14. Márquez Contreras E, Casado Martínez JJ, Pardo Alvarez J, Vázquez I, Guevara B, et al. (2006) [Prevalence of white-coat hypertension and masked hypertension in the general population, through home blood pressure measurement]. Aten Primaria 38: 392-398.

15. Kawabe H, Saito I (2007) Reproducibility of masked hypertension determined from morning and evening home blood pressure measurements over a 6-month period. Hypertens Res 30: 845-851.

16. Palatini P, Winnicki M, Santonastaso M, Mos L, Longo D, et al. (2004) Prevalence and clinical significance of isolated ambulatory hypertension in young subjects screened for stage 1 hypertension. Hypertension 44: 170-174.

17. Lurbe E, Torro I, Alvarez V, Nawrot T, Paya R, et al. (2005) Prevalence, persistence, and clinical significance of masked hypertension in youth. Hypertension 45: 493-498.

18. Trudel X, Milot A, Brisson C (2013) Persistence and progression of masked hypertension: a 5-year prospective study. Int J Hypertens 2013: 836387.

19. Viera AJ, Hinderliter AL, Kshirsagar AV, Fine J, Dominik R (2010) Reproducibility of masked hypertension in adults with untreated borderline office blood pressure: comparison of ambulatory and home monitoring. Am J Hypertens 23: 1190-1197.

20. Verberk WJ, Thien T, Kroon AA, Lenders JW, van Montfrans GA, et al. (2007) Prevalence and persistence of masked hypertension in treated hypertensive patients. Am J Hypertens 20: 1258-1265.

21. Myers MG, Godwin M, Dawes M, Kiss A, Tobe SW, et al. (2012) The conventional versus automated measurement of blood pressure in the office (CAMBO) trial: masked hypertension sub-study. J Hypertens 30: 1937-1941.

22. Cacciolati C, Hanon O, Dufouil C, Alpérovitch A, Tzourio C (2013) Categories of hypertension in the elderly and their 1-year evolution. The Three-City Study. J Hypertens 31: 680-689.

23. Banegas JR, Ruilope LM, de la Sierra A, de la Cruz JJ, Gorostidi M, et al. (2014) High prevalence of masked uncontrolled hypertension in people with treated hypertension. Eur Heart J .

24. Hermida RC, Ayala DE, Mojón A, Fernández JR (2012) Sleep-time blood pressure and the prognostic value of isolated-office and masked hypertension. Am J Hypertens 25: 297-305.

25. Sega R, Trocino G, Lanzarotti A, Carugo S, Cesana G, et al (2001) Alterations of cardiac structure in patients with isolated office, ambulatory, or home hypertension: Data from the general population (Pressione Arteriose Monitorate E Loro Associazioni [PAMELA] Study). Circulation 104:1385-1392.

26. Ishikawa J, Ishikawa Y, Edmondson D, Pickering TG, Schwartz JE (2011) Age and the difference between awake ambulatory blood pressure and office blood pressure: a meta-analysis. Blood Press Monit 16: 159-167.

27. Konstantopoulou AS, Konstantopoulou PS, Papargyriou IK, Liatis ST, Stergiou GS, et al. (2010) Masked, white coat and sustained hypertension: comparison of target organ damage and psychometric parameters. J Hum Hypertens 24: 151-157.

28. Barochiner J, Cuffaro PE, Aparicio LS, Alfie J, Rada MA, et al. (2013) Predictors of masked hypertension among treated hypertensive patients: an interesting association with orthostatic hypertension. Am J Hypertens 26: 872-878.

29. Uzu T, Nakao K, Kume S, Araki H, Isshiki K, et al. (2012) High sodium intake is associated with masked hypertension in Japanese patients with type 2 diabetes and treated hypertension. Am J Hypertens 25: 1170-1174.

30. Mancia G, Bombelli M, Facchetti R, Madotto F, Quarti-Trevano F, et al. (2009) Increased long-term risk of new-onset diabetes mellitus in white-coat and masked hypertension. J Hypertens 27: 1672-1678.

31. Sehestedt T, Jeppesen J, Hansen TW, Rasmussen S, Wachtell K, et al. (2012) Can ambulatory blood pressure measurements substitute assessment of subclinical cardiovascular damage? J Hypertens 30: 513-521.

32. Hänninen MR, Niiranen TJ, Puukka PJ, Kesäniemi YA, Kähönen M, et al. (2013) Target organ damage and masked hypertension in the general population: the Finn-Home study. J Hypertens 31: 1136-1143.

33. Terawaki H, Metoki H, Nakayama M, Ohkubo T, Kikuya M, et al. (2008) Masked hypertension determined by self-measured blood pressure at home and chronic kidney disease in the Japanese general population: the Ohasama study. Hypertens Res 31: 2129-2135.

34. Santulli G, Cipolletta E, Sorriento D, Del Giudice C, Anastasio A, et al. (2012) CaMK4 Gene Deletion Induces Hypertension. J Am Heart Assoc 1: e001081.

35. Santulli G, Trimarco B, Iaccarino G (2013) G-protein-coupled receptor kinase 2 and hypertension: molecular insights and pathophysiological mechanisms. High Blood Press Cardiovasc Prev 20: 5-12.

36. Kurnik D, Muszkat M, Sofowora GG, Friedman EA, Dupont WD, et al. (2008) Ethnic and genetic determinants of cardiovascular response to the selective alpha 2-adrenoceptor agonist dexmedetomidine. Hypertension 51: 406-411.

37. Björklund K, Lind L, Zethelius B, Andrén B, Lithell H (2003) Isolated ambulatory hypertension predicts cardiovascular morbidity in elderly men. Circulation 107: 1297-1302.

38. Ohkubo T, Kikuya M, Metoki H, Asayama K, Obara T, et al. (2005) Prognosis of “masked” hypertension and “white-coat” hypertension detected by 24-h ambulatory blood pressure monitoring 10-year follow-up from the Ohasama study. J Am Coll Cardiol 46: 508-515.

39. Mancia G, Bombelli M, Facchetti R, Madotto F, Quarti-Trevano F, et al. (2009) Long-term risk of sustained hypertension in white-coat or masked hypertension. Hypertension 54: 226-232.

40. Wang YC, Koval AM, Nakamura M, Newman JD, Schwartz JE, et al. (2013) Cost-effectiveness of secondary screening modalities for hypertension. Blood Press Monit 18: 1-7.