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REVIEW

Masked Hypertension: A Systematic Review

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Background Masked phenomenon, Masked Hypertension (MHT) and Masked Uncontrolled Hypertension (MUCH) is a well-defined clinical entity. However, many aspects of MHT/MUCH remain unclear.

Methods We systematically reviewed the published literature on MHT/MUCH from 1 January 2000 to 31 June 2018 with a particular focus on epidemiology, clinical significance, evaluation and management. Meta-analyses were performed with respect to prevalence, clinical significance and diagnostic agreement between home blood pressure (HBP) and ambulatory BP (ABP) measurements.

Results The overall weighted-mean prevalence of masked phenomenon was 11% [9,14]; MHT 10% [9,11]; and MUCH 13% [8,17]. The weighted-mean prevalence when expressed as a proportion of patients with normal office BP was 32% [25,40]; MHT 28% [15,41]; and MUCH 43% [29,57]. The prevalence of masked phenomenon determined by ABP (11% [8,14]) and HBP (13% [9,16]), was similar. However, ABP appeared to have a greater sensitivity, i.e. proportion of patients diagnosed as having MHT/MUCH was greater with ABP than with HBP (22% v 16%, $p < 0.05$), when both methodologies were applied to the same cohort of patients. The prevalence of MHT was influenced by ethnicities and comorbidities, and in case of MUCH by anti-hypertensive treatment. MHT/MUCH was associated with increased risk of fatal and non-fatal cardiac/cerebrovascular events (relative risk [RR] 2.09 [1.80, 2.44]), and the risk was comparable to sustained hypertension (SHT) (RR 2.26 [1.84, 2.78]). The increased risk occurred regardless of the method of out of office BP assessment; the relative risks for ABP and HBP were 2.38 [1.90, 2.98] and 1.90 [1.57, 2.29] respectively. The diagnostic agreement between ABP and HBP was only modest, kappa = 0.46 [0.40, 0.52], even though the percentage agreement was 83%. The evidence for the management of MHT was scant.

Conclusions MHT/MUCH is a common BP phenotype with a risk profile similar to that of SHT. Therefore, high risk patients should undergo out of office BP assessment, probably both by HBP and ABP, to confirm diagnosis and be considered for treatment.

Keywords Masked hypertension • Masked uncontrolled hypertension • Ambulatory blood pressure • Home blood pressure • Masked phenomenon

Introduction

Hypertension remains a major cause of cardiovascular morbidity and mortality worldwide. The introduction of ambulatory blood pressure (ABP) monitoring has led to the identification of four patterns of blood pressure (BP) phenotypes, i.e. sustained normotension (NT), sustained hypertension (SHT), white coat hypertension (WCHT) and

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masked hypertension (MHT). In 2002, Pickering coined the term MHT; MHT or masked uncontrolled hypertension (MUCH) is defined as a person having normotensive office blood pressure (OBP) and hypertensive out of office blood pressure. The term MHT is reserved for treatment naïve patients and MUCH for patients with treated hypertension. Although the recent emphasis on out of office BP measurement has led to the masked phenomenon being increasingly recognised, there is a lack of awareness of this phenomenon amongst practitioners. Furthermore, many aspects of this phenomenon remain unclear. This study systematically reviews the published literature on MHT/MUCH with a particular focus on epidemiology, clinical significance, evaluation/diagnosis and management. The search methodology was in accordance with PRISMA guidelines [1].

Methods

Definitions/Terminologies

Masked hypertension and MUCH are reserved for untreated and treated patient groups, respectively, in this review, although these terms were interchangeably used in the literature. The term 'masked phenomenon' or 'MHT/MUCH' refers to out of office hypertension in combined treated and untreated or mixed patient groups.

Search Strategy

Medline (OvidSP), PubMed and Cochrane databases were searched for articles published in English language from 1 January 2000 to 30 June 2018. The following individual terms were used: ''masked hypertension'' (MeSH), ''masked hypertension (keyword)'', ''masked uncontrolled hypertension'' (keyword), ''reverse white coat hypertension'' (keyword), ''out of office hypertension'' (keyword), ''ambulatory hypertension'' (keyword) and ''white coat normotension'' (keyword). All publications except case reports, editorials, comments, reflections, letters, book chapters, narrative reviews and studies in paediatric age group were included. Full text versions of the eligible articles were reviewed by two authors (HT and MA) independently and disagreements were resolved by consensus, or by discussion with the third author (AP), if there was ambiguity regarding statistical methodology or reporting. If multiple references were available for a specific citation, references were chosen based on their following attributes: prospective study design with a control group; largest and/or random selection of sample; and the longest follow-up. Similarly, when two or more articles reported results from the same cohort or overlapping cohorts, the one with the longest follow-up or largest sample size was included, unless they had used different out of office BP methodologies or definitions for diagnosing MHT/MUCH, or reported on different clinical outcomes. Meta-analyses were performed to determine the following: weighted-mean prevalence of masked phenomenon as well as MHT and MUCH; the estimated relative risk (RR) of composite cardiovascular and/or cerebrovascular risk of MHT/MUCH; and the diagnostic agreement between ABP and HBP measurements for diagnosing MHT/MUCH. For the estimate of prevalence, studies that reported the prevalence or provided enough information to calculate this and had a sample size of at least 500 were included. The inclusion criteria for the estimation of adverse outcomes included cohort studies in the general or hypertensive populations that reported fatal and non-fatal cardiovascular and/or cerebrovascular events. Studies that had samples predominantly representing specific comorbidities such as chronic kidney disease (CKD) or type 2 diabetes mellitus (T2DM), or reported only surrogate clinical outcomes were not included. To be included in the analysis of diagnostic agreement between ABP and HBP, studies should have provided either a kappa statistic or adequate information for its estimation.

Statistical Methods

Estimates of statistics pooled across subgroups of the studies were computed using random effects models estimated by restricted maximum likelihood (REML). The resulting estimates are weighted means of study estimates, with weighting given by the precision of the estimate. Precision is the reciprocal of the variance (which is the square of the standard error). Confidence intervals (95%) were obtained from the corresponding random effects model, and shown in square brackets following the estimated value of a statistic. In a random effects meta-analysis, the I-squared statistic is defined as the ratio of total heterogeneity to total variance; a Q-statistic can also be defined, which leads to a test of the null hypothesis of homogeneity. Where appropriate, we reported these values or test outcomes. All analysis (including the forest plots) was carried out in the R statistical language [2], using the *metafor* package [3], and further information about the models and forest plots can be found in the latter reference.

Results

The search generated 625 articles. We excluded 368: 69 (duplicates); 6 (editorials); 102 (narrative reviews); 3 (case reports); 64 (paediatric studies), 1 (active trial) and 123 (a miscellaneous group consisting of comments, reflections, letters, etc.). Of the 257 articles included, 128 were in untreated patients, 66 in treated patients and 63 included both treated and untreated patients. The study designs consisted of cross-sectional in 37; case control in 61; cohort in 145; randomised controlled trial (RCT) in 4; and systematic review/meta-analysis in 10. Office blood pressure methodology was manual in 154, automated in 77, and not specified in 16. Out of office BP methodologies included ABP in 172, home BP (HBP) in 52 and home and ABP in 23 studies. Eighty-one (81) articles predominantly described epidemiology, 7 pathogenesis, 82 clinical significance, 70 evaluation/diagnosis, and 7 management. Thirty-three (33) articles described more than one aspect of MHT/MUCH (Figure 1).

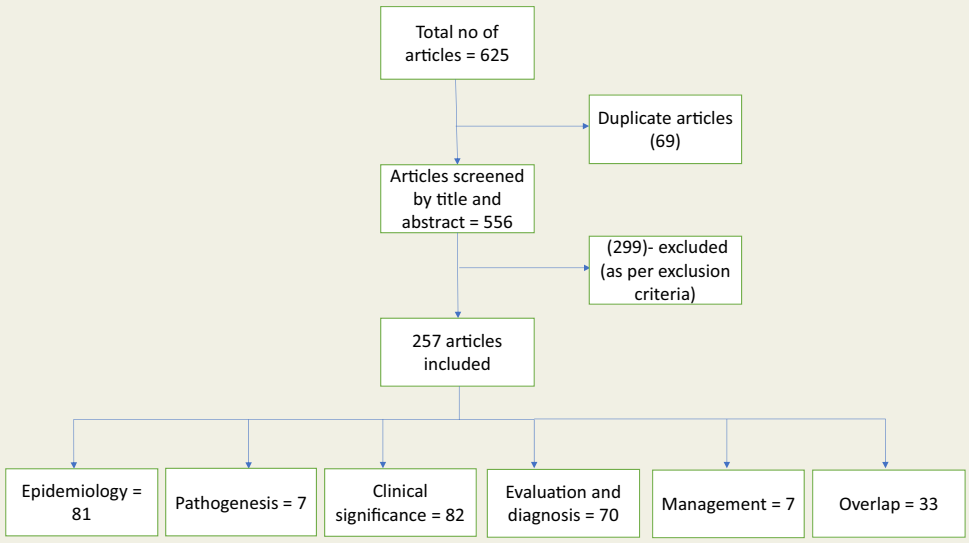

Figure 1 Flowchart of search methodology.

Epidemiology

Prevalences

We included 16 studies [4–19] in the meta-analysis; 10 studies had both treated and untreated patients [4,7,9–14,17,19], four had untreated [5,6,15,18] and two had treated patients [8,16]. Moreover, of the 10 studies with mixed patients, it was possible to segregate untreated and treated patients in three studies [4,10,13]. The total number of participants was 103,802: 39,103 untreated, 54,618 treated, with 10,081 unable to be determined as treated or untreated. The weighted-mean prevalences using either daytime or 24-hour ABP, or HBP to define out of office BP were as follows: masked phenomenon 11% [9,14]; MHT 10% [9,11]; and MUCH 13% [8,17] (Figure 2). The weighted-mean prevalences when masked phenomenon was expressed as a proportion of patients with normal office BP (i.e. the sum of NT and MHT or MUCH) were: masked phenomenon 32% [25,40]; MHT 28% [15,41]; and MUCH 43% [29,57]. The weighted-mean prevalences (expressed as a proportion of study sample size) using ABP versus HBP for out of office BP assessment were 11% [8,14] and 13% [9,16], respectively (Figure 2). These, when expressed as a proportion of patients with normal OBP, were 32% [21,44] and 27% [17,37], respectively for ABP and HBP (Figure 2).

As can be seen, the confidence intervals of the weighted-mean prevalences were wide, indicating large variations in the reported prevalences between studies. For the prevalences measured as a proportion of study sample size and as a proportion of those with normal OBP, respectively, the I-squared statistics were 99.64% and 99.59%. This heterogeneity was probably ascribable to varying population characteristics, including comorbidities and ethnicities, in different studies. The varying definitions of MHT/MUCH, methodological differences in out of office BP assessment (HBP v ABP) and whether the prevalence of MHT/MUCH was expressed as proportion of total study sample or as a proportion of patients with normal OBP were also contributory. Most earlier studies used the mean daytime ABP [4,9,11,14,15] to define MHT/MUCH, whereas recent studies, because of prognostic significance of nocturnal hypertension [10,19,20], included either the 24-hour mean or any one of the three ABP means in their definition. As expected, studies that adopted either of the three ABP means to define MHT reported a higher prevalence [21]. Similarly, as observed in this analysis, studies that reported the prevalence as a proportion of patients with normal office BP also reported a higher prevalence (Figure 2).

The Effect of Ethnicities

The prevalence of MHT was high in patients of African descent; sub-Saharan Africans up to 18% [22] and African-Americans up to 52.25% [23], whereas it was low in Korean (5.7%) [14] and Omani (6%) [24] populations. While the high prevalence in African descent may be due to the presence of concomitant comorbidities such as diabetes and CKD, the reasons for the low prevalence in Korean and Omani ethnicities are unclear. The prevalence of MHT was also studied in other ethnic groups, with two studies implicating high sodium intake for the increased prevalence in Japanese [25] and Chinese populations [15].

The Effect of Comorbidities

The influence of comorbidities on the prevalence of MHT/MUCH was particularly evident in diabetes [26] and CKD [27]. A high prevalence of up to 30% was described in obstructive sleep apnoea (OSA) [28], largely due to the presence of NHT, but was investigated in only two studies. The prevalence in diabetics was between 13.3% [26] and 66.4% [25] and in CKD was between 7% [27] and 32.8% [29]. There was only one study in haemodialysis patients reporting a prevalence of 15% [30]. There were no studies in peritoneal dialysis patients, but three studies reported a prevalence between 16% [31] and 39% [32] in renal transplant recipients.

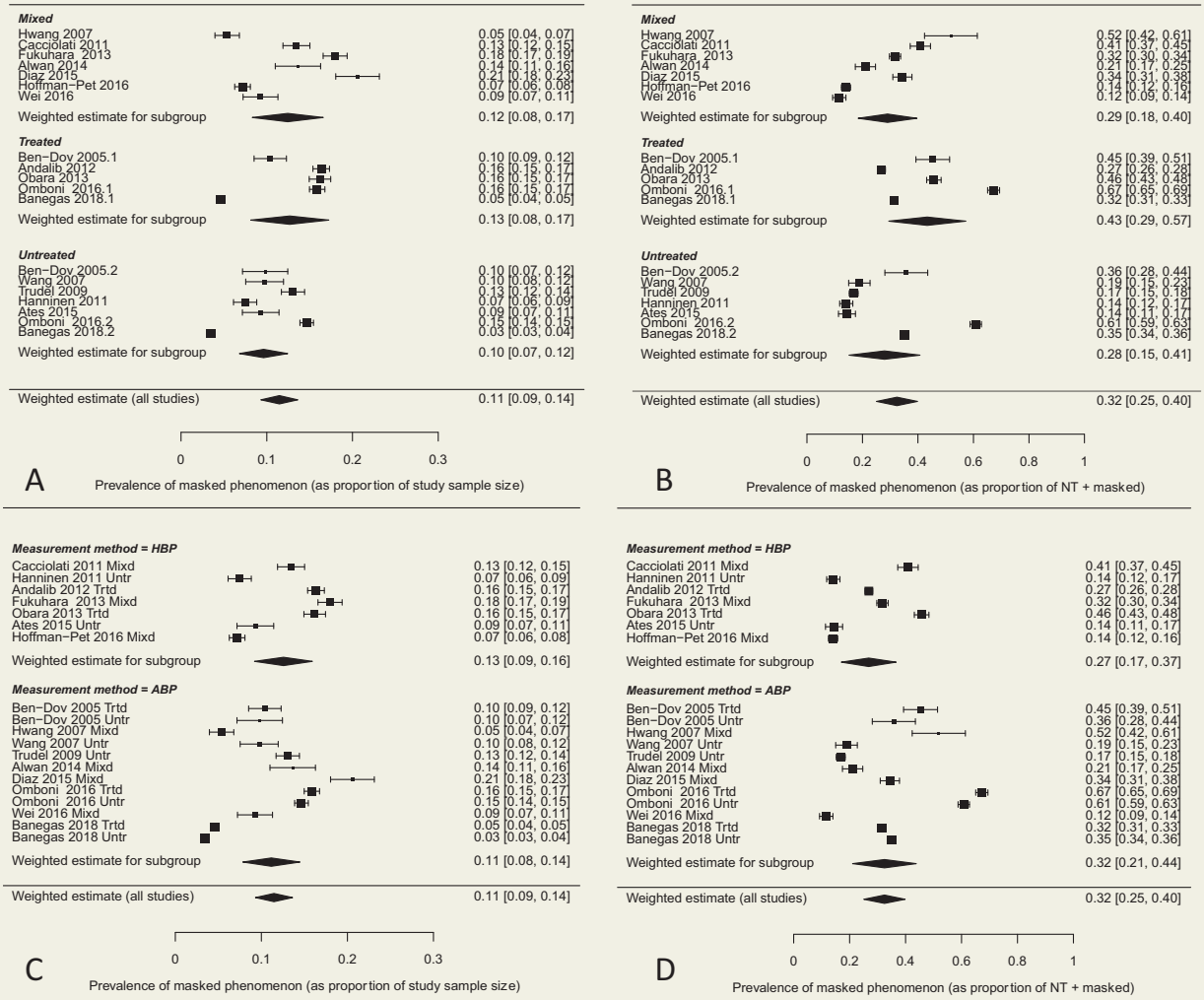

Figure 2 Prevalence of Masked Hypertension (MHT) and Masked Uncontrolled Hypertension (MUCH).
A: Studies grouped by treatment status. Masked phenomenon is depicted as a proportion of the study sample size. For studies with both treated and untreated groups separately, the number after the year (as in 2005.1) indicated separate samples in the same paper. For each study the following are shown: a filled square, located at the study estimate, with size proportional to the precision (= 1/(SE squared)) of the estimate and a 95% confidence interval. The diamond for the weighted estimate is the combined random effects (precision-weighted) estimate with the left and right extents showing its 95% confidence interval. Also on the right are shown the estimate values with 95% confidence intervals.
B: Studies grouped by treatment status. Masked phenomenon is depicted as a proportion of subjects with normal office blood pressure (BP).
C: Studies grouped by method of out of office blood pressure (BP) measurement, ABP (ambulatory BP) and HBP (home BP) measurement. Masked phenomenon is depicted as a proportion of study sample size.
D: Studies grouped by method of out of office blood pressure (BP) measurement. Masked phenomenon is depicted as a proportion of subjects with normal office BP.

There was one study in prospective renal donors reporting a prevalence of 17% [33].

Masked Phenomenon in Special Groups

Studies have described an increased prevalence of MHT in young and middle-aged healthy cohorts. Trachsel et al. reported a 38% prevalence of MHT in 87 middle aged endurance athletes with normal office BP, where MHT was associated with left ventricular diastolic dysfunction and structural changes [34]. Berge et al. reported a prevalence of 35% among 26 healthy football players [35]. Although the reported structural cardiac changes cannot be ignored, these findings in young athletes need to be interpreted with caution. The sample sizes were small and the studies did not control for confounders such as cardiovascular changes associated with endurance exercise, such as spurious isolated systolic hypertension [36] and post exercise hypotension [37]. Other physical and psychosocial factors such as work-related stress and use of alcohol and medications were also not included in the analysis. Masked hypertension was also described in

white collar workers with a prevalence between 15% [5] and 24% [38]. This may be due to a combination of mental stress and poor exercise tolerance and hypertensive response to low intensity exercise during day's activities when out of office BP is measured, with normal or pre-hypertensive BP values at rest when OBP is measured [39]. A prevalence of MHT up to 16% was reported in older people [7], probably due to the high prevalence of BP variability and postprandial hypotension. People with smoking, excessive alcohol consumption and substance abuse also had a high prevalence of MHT [5] because they often record a lower OBP as a result of being abstinent when visiting doctors.

Association Between Treatment of Hypertension and MUCH

Studies have consistently shown an association between treatment of hypertension and MUCH [40]. This may be because of the apparent greater BP reduction effect of antihypertensive treatment on OBP compared to ABP resulting in a proportion of patients with sustained hypertension being converted to MUCH rather than sustained NT [41]. This phenomenon could be explained at least in part by the methodology of BP measurement, as OBP, which is routinely used for BP control and treatment efficacy, is not capable of assessing night time and pre-awakening BP. Furthermore, OBP is often taken at the time of peak action of anti-hypertensives, thus recording a lower OBP.

Clinical Significance

Masked hypertension has often been shown to progress to sustained hypertension (SHT) including in older people [42] and confers a cardiovascular risk almost similar to sustained hypertension [13] in both the general population and in patients with diabetes and CKD [43].

Ten (10) studies [13,23,44–51] met the criteria for inclusion in the meta-analysis undertaken to estimate the relative risk of composite fatal and non-fatal cardiac and/or cerebrovascular events associated with MHT/MUCH. The total number of patients with either MHT or MUCH was 8,295. The total number of patients with sustained NT and SHT were 19,069 and 37,220, respectively. Patients with SHT were identified from 8 of these 10 studies, as two [23,46] included only patients with normal office BP. Patients with MHT/MUCH were 2.09 [1.80,2.44] times more likely to suffer adverse cardiovascular and/or cerebrovascular events compared to patients with sustained NT (Figure 3). This relative risk was quite similar to patients with SHT, RR 2.26 [1.84,2.78] (Figure 3). Out of office BP assessment was undertaken by ABP in 6,243 patients and HBP in 2,052 patients. When the risk of adverse outcomes was assessed by the modality of out of office BP assessment, ABP and HBP conferred a comparable RR; RRs for masked phenomenon assessed by ABP and HBP were 2.38 [1.90,2.98] and 1.90 [1.57, 2.29], respectively (Figure 3). The tests of homogeneity based on the Q-statistic in all cases showed a p-value much greater than 0.05, indicating that the null hypothesis of homogeneity was not rejected.

Most previous studies [52,53], in keeping with the results of the present analysis, have confirmed that MHT/MUCH had an increased cardiovascular risk that is similar to SHT. Studies have also shown that the increased risk is regardless of the method of out of office BP assessment [54,55]. In the present analysis, although RR assessed by ABP was higher than for HBP, this at best was only marginally significant.

Besides patient relevant outcomes, studies have also shown a significant association between masked phenomenon and surrogate cardiovascular outcomes, such as left ventricular hypertrophy, increased carotid intima-media thickness, albuminuria, aortic stiffness, high pulse wave velocity, silent cerebral infarcts and early hypertensive retinal changes in patients with MHT/MUCH [49,56–59].

Evaluation and Diagnosis

A reliable diagnosis of MHT/MUCH requires accurate measurement of office and out of office blood pressures. The evidence regarding OBP measurement is consistent and there is strong agreement for using automated devices in preference to manual devices [60]. However, this is not the case with regard to out of office BP measurements. Although a number of studies and systematic reviews have compared the performance of ABP and HBP for diagnosing sustained hypertension and predicting clinical outcomes, only a few have compared them for diagnosing MHT/MUCH. We identified 12 studies [61–72] and one meta-analysis [73] that undertook some form of comparison of the diagnostic performance of ABP and HBP for diagnosing MHT/MUCH. Of these, four studies [69–72] and the meta-analysis merely compared the prevalence of MHT/MUCH diagnosis by each method without providing any measure of diagnostic agreement or bias between the two methods. While two of these [70,73] found no difference in the prevalence of MHT/MUCH diagnosis by either method, three [69,71,72] found that ABP diagnosed MHT/MUCH in a significantly greater proportion of patients. Of the remaining eight studies, seven studies also provided, along with other measures of comparison such as percentage agreement, Bland-Altman analysis etc., either Cohen's kappa statistic or adequate information to calculate it [61–64,66–68], and is therefore included in the meta-analysis. One study [65] was not included in the meta-analysis as it provided only details of Bland-Altman analysis without providing enough information for estimating kappa statistics.

The results of the meta-analysis of kappa statistics showed that the overall diagnostic agreement between ABP and HBP was only modest (kappa = 0.46 [0.40,0.52]) (Figure 4); the I-squared statistic was 64% and the p-value for the Q-statistic test of homogeneity was 0.005, indicating inhomogeneity. The proportion of patients diagnosed as having MHT/MUCH was greater with ABP than with HBP (22% v 16%, $p < 0.05$). These percentages were obtained by a meta-analysis involving extraction of the corresponding sample counts by algebraic solution (where needed) of equations based on combinations of sensitivity, percentage agreement, kappa,

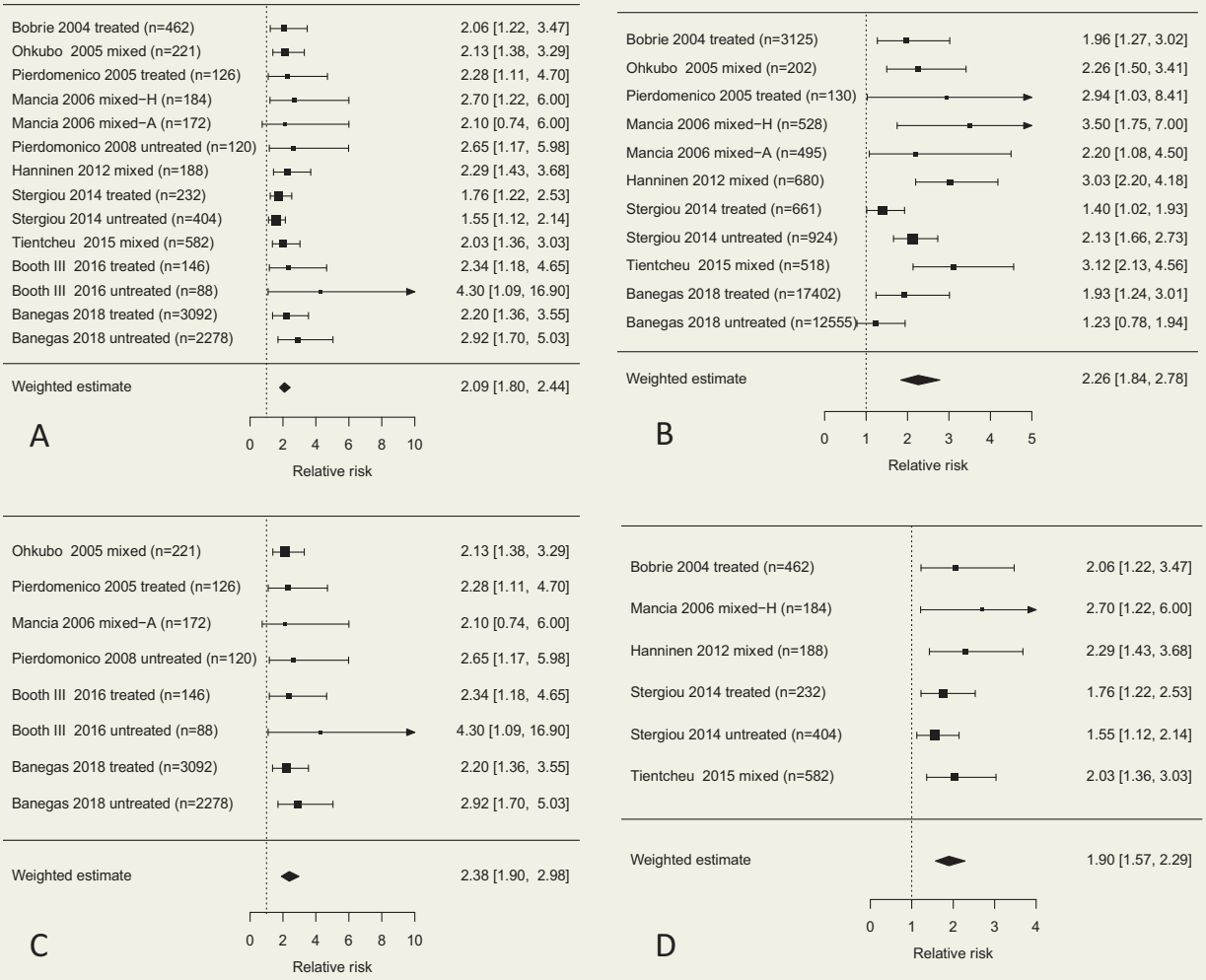

Figure 3 Relative risk (RR) for fatal and non-fatal cardiovascular/cerebrovascular events.
A: RR in masked phenomenon.
B: RR in sustained hypertension.
C: RR when masked phenomenon was diagnosed by ambulatory blood pressure (BP).
D: RR when masked phenomenon was diagnosed by home blood pressure (BP).

etc. as reported in the seven studies shown in (Figure 4). The percentage agreement was obtainable in the same way from these seven studies and the overall percentage agreement was 83% [82,84]. Bland-Altman analysis was undertaken in two studies [65,67] and the results demonstrated a statistically significant diagnostic disagreement between HBP and ABP with an overall tendency for HBP to report a higher BP compared with ABP. However, the conclusion to be drawn here is not simple as Nascimento et al. demonstrated that the bias was not constant across the range of observed BP values, being in the opposite direction at lower BPs.

The modest agreement seen in this analysis is consistent with other studies [74]. This is not unexpected as BP is measured by ABP and HBP differently and under different circumstances, and therefore they provide somewhat different information on patient's BP. Our findings further suggest that, although the rates of prevalence of MHT/MUCH determined by both ABP and HBP were comparable, ABP had a greater sensitivity for diagnosing MHT/MUCH, if ABP and HBP were used to diagnose MHT/MUCH in the same cohort of patients. This may be because HBP lacks night time and 24-hour BP readings. Although the greater sensitivity for ABP has been shown by previous studies, we are not aware that this has been demonstrated in a meta-analysis. The finding that ABP had a greater sensitivity than HBP for diagnosing MHT/MUCH is at odds with the results of the Bland-Altman analysis undertaken by Nascimento et al. and Muxfeldt et al. as their results show an overall tendency for HBP to report a higher BP compared with ABP for a given patient [65,67]. These observations are difficult to reconcile, although the Bland-Altman analysis by Nascimento et al. appears to show that at lower end of BP values, ABP is likely to overestimate the BP.

Besides comparing BP methodologies, studies have also investigated the optimal BP monitoring schedules for diagnosing MHT/MUCH such as the number and frequency of

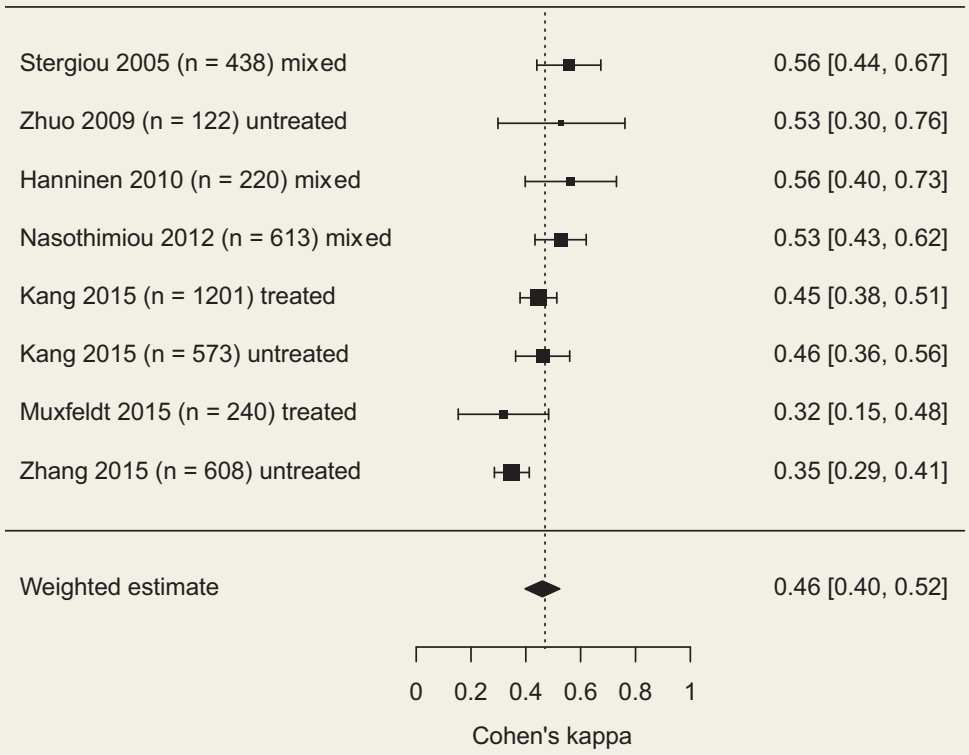

Figure 4 Diagnostic agreement between ambulatory blood pressure (ABP) and home blood pressure (HBP). Estimates of Cohen's kappa for diagnosing masked phenomenon using either ambulatory BP monitoring or home BP monitoring. For each study, the estimate plus a 95% confidence interval is shown. Overall weighted estimate is shown beneath.

BP measurements. As far as the office and home BP measurements are concerned, the evidence suggests that a reliable diagnosis of MHT/MUCH would require OBP in duplicate or triplicate measurements taken over at least two visits, 2 to 4 weeks apart [75,76] and HBP twice daily in in duplicate measurements over 4 to 6 consecutive days [75]. Unlike OBP and HBP schedules, there was only limited information available for ABP measurement schedule for diagnosing MHT/MUCH. Although most studies have used only one ABP measurement, the Conventional versus automated measurement of blood pressure in the office (CAMBO) trial suggests that at least two ABP measurements would be required for a firm diagnosis of MHT [60].

Management

We identified seven interventional studies; two for MHT and five for MUCH. Drager et al. [77] found that CPAP decreased the frequency of MHT in patients with OSA in a randomised controlled trial in a sample of 40 patients. However, this was not replicated by Sova et al. in a study of 43 patients [78].

There were no studies of pharmacological interventions available for MHT, although one is currently underway (NCT02142881). There were five open label studies for MUCH. Of these, three were from the same group of investigators, namely the Home blood pressure measurement with Olmesartan naive patients to establish standard target blood pressure (HONEST) study group. They essentially demonstrated that antihypertensive regimens using long acting medications and combination treatment were more effective in improving BP control. They found that adding olmesartan, a long acting angiotensin receptor blocker, to the current drug regimen converted patients with MUCH to normotension largely by improving the morning BP surge [79,80]. This approach was found to be effective in the elderly as well [81], although clinical outcomes were not assessed by these studies. Girerd et al. demonstrated that combination treatment with valsartan and hydrochlorothiazide was more effective in improving MUCH [82]. Kario et al. [83] found that azelnidipine, a long acting calcium channel blocker, alone or in combination improved the pulse rate and morning BP surge in MUCH.

Conclusion and Perspectives

Masked hypertension/MUCH as a well-defined clinical entity and its association with adverse clinical outcomes are clearly established by the current body of evidence, including the present review. The results of the present review suggest that approximately one in three patients, untreated or treated, recording a normal OBP, is likely to have MHT or MUCH regardless of the out of office BP methodology used. However, from a clinical viewpoint, there are many unresolved issues regarding the diagnosis and management of this phenomenon.

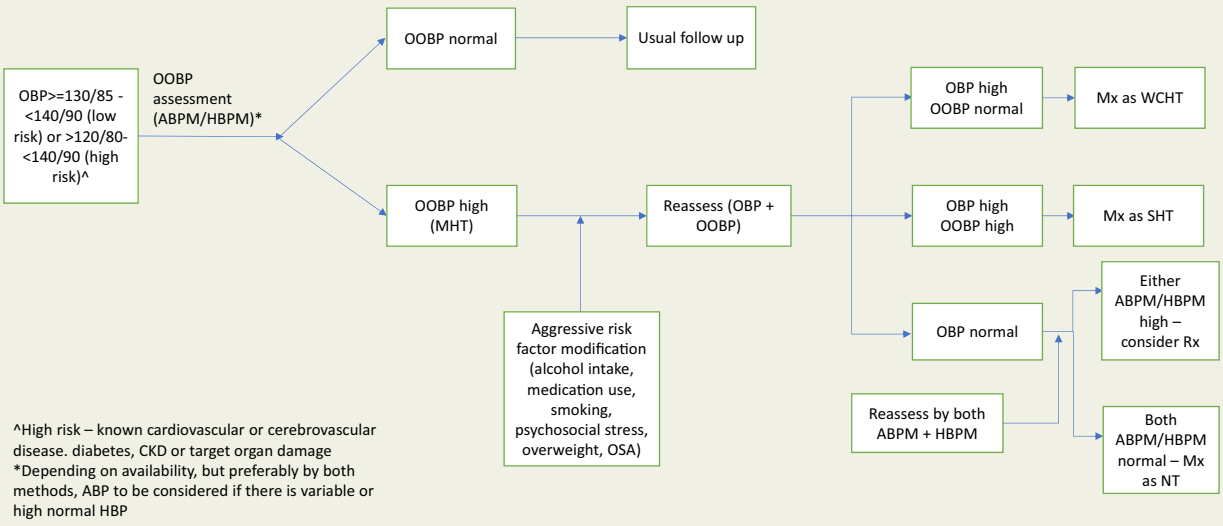

Figure 5 Diagnostic and management algorithm for Masked Hypertension (MHT).
Abbreviations: OBP, office blood pressure; OOBP, out of office blood pressure; ABPM, ambulatory blood pressure monitoring; HBPM, home blood pressure monitoring; MHT, masked hypertension; WCHT, white coat hypertension; SHT, sustained hypertension; NT, normotension; OSA, obstructive sleep apnea.

Although ABP is generally recommended by most authorities [84,85], maybe because of its greater sensitivity, its superiority over HBP is not underpinned by evidence based on clinical outcomes [45,54,55]. Furthermore, from a practical viewpoint, HBP may be less cumbersome for patients [63] and is able to track out of office BP over days, weeks and months, which may not be logistically feasible with ABP. Therefore, there is lack of strong empirical evidence to recommend ABP or HBP over the other. In view of these considerations and given the significant diagnostic disagreement between ABP and HBP for diagnosing MHT/MUCH, we believe that patients should undergo assessment by both methods to confirm diagnosis (Figure 5). This is likely to improve the overall rate of diagnosis that may translate into improved patient outcomes because diagnosis of MHT/MUCH by either ABP or HBP, as evidenced by this review, appears to confer similar cardiovascular risk [54]. Furthermore, there is also limited evidence to suggest that patients diagnosed by both methods may be at a greater cardiovascular risk compared to those whose diagnosis was confirmed by either of these methods [45].

Another challenge regarding diagnosing MHT is the optimal and cost-effective approach to define the target group that requires assessment for MHT, as indiscriminate screening of all with normotensive office BP is not practical. Although at present there is no clinical tool available to assist clinicians with screening, a practical proposition would be to consider those with high normal OBP [13,45] and those with high cardiovascular risk [26,27] or target organ damage but with normal OBP for assessment of MHT (Figure 5).

The recent introduction of the fully automated oscillometric device, which is capable of multiple OBP measurements without the attendance of trained staff gives a whole new dimension to OBP measurement [86]. This device records a lower OBP compared to the conventional automated device that requires trained staff and correlates more strongly with daytime ABP measurements [87]. This technology is likely to have significant implications for the diagnosis of MHT, but its diagnostic utility is yet to be fully assessed. Although recording a lower OBP could be expected to increase the prevalence of MHT, the available evidence suggests that it eliminates WCHT without increasing the prevalence of MHT [60].

At present the OBP threshold <140/90 mmHg is used to define MHT/MUCH. However, this threshold may not be appropriate for all clinical situations, as the recommended OBP in patients with specific comorbidities is likely to vary. Furthermore, the results of the Systolic blood pressure intervention trial (SPRINT) trial [88] add further impetus for revising and individualising BP cut points for defining MHT/MUCH.

The benefit of treating MHT, especially pharmacologically, remains speculative, as this hypothesis is yet to be tested in controlled settings. However, if one follows the argument that MHT confers a similar cardiovascular risk to that of SHT, pharmacologic treatment at least in the high-risk patients may be justified. Therefore, while we await the results of RCTs in MHT, we believe that it would be reasonable to consider pharmacologic treatment in high risk patients, but only after optimisation of patient's metabolic profile and other potential risk factors including psychosocial and work-related stress. A thorough search for personalised risk factors is important in all patients, especially in the young without any obvious risk factors (Figure 5).

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