Masked hypertension: A common but insidious presentation of hypertension

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A patient has masked hypertension when his office blood pressure is less than 140/90 mmHg but his ambulatory or home blood pressure readings are in the hypertensive range. Several recent studies have demonstrated that cardiovascular risk is similar between those with masked hypertension and those with sustained hypertension. The prevalence of masked hypertension in Canada is not known, but data from other countries suggest rates greater than 8%. Physicians need to use careful clinical judgment to identify and treat subjects with masked hypertension. The present review discusses masked hypertension, its importance to clinical practice and some aspects of patient management.

Key Words: Ambulatory; Blood pressure; Home; Hypertension; Masked; Office

Masked hypertension (MH) is strongly linked to an increased risk of heart disease and stroke (1-4). Mounting evidence suggests that MH must be taken into account in the assessment of blood pressure (BP), but little is known about how masked hypertensive patients are identified or how they should be managed. Despite prevalence estimates of at least 8% to 10% in the general population and a prognosis similar to sustained hypertension, the term, the meaning and the importance of MH are not widely understood. The present article provides some background on MH, describes its clinical importance and discusses some aspects of management in clinical practice.

What is MH?

MH is present when a normal office BP (OBP) is recorded in a patient with ambulatory BP (ABP) or home BP (HBP) readings in the hypertensive range (5). As the term implies, the hypertension is real but is masked to the physician. Patients with this condition have a normal or, more commonly, high normal OBP of less than 140/90 mmHg. Although ABP and HBP testing is not performed routinely in patients whose BP is less than 140/90 mmHg, various research studies have examined the relationship between normal OBP and ABP or HBP

L'hypertension masquée : Une présentation courante mais insidieuse

Un patient souffre d'hypertension masquée lorsque sa tension artérielle en cabinet est inférieure à 140/90 mmHg mais que ses lectures de tension artérielle ambulatoires ou à domicile figurent dans la plage de l'hypertension. Plusieurs études récentes démontrent que le risque cardiovasculaire est semblable chez les personnes qui souffrent d'hypertension masquée et celles qui souffrent d'hypertension soutenue. On ne connaît pas la prévalence d'hypertension masquée au Canada, mais les données d'autres pays laissent supposer des taux supérieurs à 8 %. Les médecins doivent faire preuve d'un jugement clinique rigoureux pour repérer et traiter les sujets atteints d'hypertension masquée. La présente analyse traite de l'hypertension masquée, de son importance en pratique clinique et de certains aspects de la prise en charge des patients.

in a variety of populations. Over the past three years, four large, prospective studies (1-4) have reported that patients with MH exhibit a risk profile similar to those who have sustained hypertension.

However, many health care professionals are unfamiliar with the concept of MH. This is possibly because of inconsistent nomenclature in the scientific or medical literature. However, the phenomenon of MH is not new. The classic paper on ABP monitoring was written by Perloff et al in 1983 (6), and demonstrated not only the superiority of ABP over OBP in predicting clinical outcomes, but also showed poorer outcomes in patients who had higher ABP values compared with their borderline or mildly hypertensive OBP. Since then, others who have observed this same phenomenon have called it a variety of names, including white coat normotension (7), reverse white coat (8), inverse white coat (9), home or isolated home hypertension (7,10), isolated ambulatory hypertension (11), isolated uncontrolled hypertension at home (12) and occult office hypertension (13). Pickering et al (5) suggested the term 'masked hypertension', and this term appears to have become the standard terminology to describe patients who have a normal OBP but elevated HBP or ABP.

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Figure 1) Cardiovascular morbidity event rates per 100 person-years in normotensive (NT), masked hypertensive (HT) and sustained HT subjects. Adapted from reference 2

What is the risk associated with MH?

Several prospective studies have concluded that the increased cardiovascular risk associated with MH is considerable. In a recent report of the Ohasama study in Japan by Ohkubo et al (3), the relative hazard (RH) index for a composite variable of cardiovascular mortality and stroke morbidity showed similar values for MH ($RH_{MH}=2.13$) and sustained hypertension ($RH_{sustainedHT}=2.26$), whereas the index for white coat hypertension ($RH_{whitecoat}=1.28$) was not statistically different from those with sustained normotension. Regardless of whether out-of-office BP is measured by HBP or ABP, the risk of experiencing a cardiovascular event is similar to that observed in patients with sustained hypertension (Figure 1). These findings strengthen the observations from numerous earlier cross-sectional studies that linked MH with target organ damage (14,15). Taken together, it is clear that both HBP and ABP predict cardiovascular risk better than OBP.

MH is a concern for certain special populations, including patients with type II diabetes, in whom damage involving the heart, blood vessels and kidneys has been observed (16). The damage associated with MH is not limited to adults, and has been reported in children and youths (17-19), in whom the finding of MH may suggest a prehypertensive state (11).

When the level of the OBP has been taken into consideration, studies reporting a link between MH and target organ damage show that OBP is commonly in the high normal range when MH is present (14,20). This finding may have clinical significance. In one study (20), when the masked hypertensive group was compared only with those normotensive subjects with systolic BP greater than 120 mmHg but less than 140 mmHg, many differences in target organ damage between the groups disappeared. Because masked hypertensive patients represented 26% of the subjects in the normal range, this finding suggests that a considerable number of patients with target organ damage may go undetected unless MH is considered or evaluated by ABP or HBP.

What is the prevalence of MH?

The prevalence of MH varies with the population studied and the specific 'cut-off points' used. Currently, there are no Canadian data, but prevalence estimates in adults range from as low as 3% (8) to as high as 49% (21). The highest prevalence

was found in a group of patients who were 'transiently hypertensive', exhibiting an elevated clinic BP at some time during their medical history. As part of a 10-year follow-up within the Ohasama study (3), the prevalence of MH in a Japanese community was 16% in untreated and 18% in treated hypertensive patients. A review of prevalence rates for MH in a number of studies has been published recently, and rates from 8% to 12% appear to be common (22).

The availability of prognostic data with 'hard' end points brought MH to the attention of the medical community (1-4). These studies showed that ABP and HBP predict risk much better than the usual clinical measurements, and that those who are found to be hypertensive by ABP or HBP have greater risk than those who are not. Logically, those with MH (ie, hypertensive ABP or HBP with normotensive OBP) should be followed in the same manner as other hypertensive patients with similar readings and risk factor profiles. The difficulty that confronts physicians and the authors of evidence-based guidelines is how to identify and manage patients who have MH.

Who should be tested for MH?

There are currently no specific characteristics that would lead one to test a patient for MH. Taken to the extreme, one could argue that every patient would benefit from having their ABP or HBP measured, but this is obviously not practical. A number of groups have tried to identify factors that may be associated with MH. Some key features linked to MH have emerged from these efforts.

The European Society of Hypertension (23) suggests that MH may be more common in younger individuals who have a high normal OBP and early left ventricular hypertrophy, in people who at some point in time have had OBP readings in the hypertensive range, and in those with a family history of hypertension in both parents, multiple risk factors for cardiovascular disease and diabetes. Whether young age is a consistent feature of MH is a matter of some disagreement (11,14,24,25), with some reports not finding this association.

In addition to the factors mentioned by the European Society of Hypertension (23), other characteristics of MH have been identified: obesity (12-15); impaired baroreflex sensitivity (20); current or past smoking (14,22,25); increased serum creatinine levels (14); increased urinary albumin excretion (16); high heart rate (24); and increased alcohol consumption (22,25). Although the list is becoming quite long, these factors, taken together, can lead one to suspect MH in a higher risk patient who may be expected to have BP readings in the hypertensive range.

How should one manage a patient with MH?

Prescribing therapy for patients with MH would seem to be the obvious conclusion from the above findings. However, there are little experimental data to support this approach. In one study involving patients with MH (26), significant improvements in left ventricular mass index and microalbuminuria were found only in those patients whose BPs were controlled according to ABP. Control of hypertension based on the OBP alone was not sufficient. At present, the treatment of patients with MH should be on an individual basis depending on clinical judgment because specific guidance awaits the results of ongoing trials (12). The expense and inconvenience of ABP measurement may limit its use in the routine management of MH. HBP measurement may be a more affordable option.

Which factors contribute to MH?

The causes of MH are almost certainly multifactorial. An OBP reading that is lower than an ABP or HBP reading could occur for a variety of reasons, including random BP fluctuations, factors that cause BP to be lower in the clinic, factors that cause home or ambulatory readings to be higher, differences in the quality of automated out-of-office versus conventional OBP measurements and the selection of cut-off points for defining hypertension.

Despite the variability of BP within or among days, the reproducibility of MH can be quite high provided that strict diagnostic criteria are met. Analysis of the results from the Self-measurement of blood pressure at Home in the Elderly: Assessment and Follow-up (SHEAF) study (27) found that triplicate office readings taken on two different days combined with at least 15 HBP values were necessary for optimum statistical analysis. Fewer office readings or fewer home readings had a major impact on the reproducibility of the data. The reproducibility of MH has also been tested in a subset of patients who underwent ABP readings twice for routine clinical indications (24). Of those with MH after the first recording, 71% had masked or sustained hypertension on the second occasion. Of those with MH on the second recording, sustained or MH was found in 80% of patients on their first test. Although HBP and ABP identify a similar prevalence of MH, the subsets of patients identified may not necessarily be the same (28). However, diagnostic disagreement may be reduced to less than 10% by raising the diagnostic threshold for ABP and HBP to 140/90 mmHg from 135/85 mmHg.

Certain factors are known to affect ambulatory readings and could contribute to higher out-of-office readings. For example, people are less likely to be smoking cigarettes, drinking coffee, engaging in physical activities or experiencing job strain when at the clinic (29).

Morning HBP readings should be taken soon after rising but before taking antihypertensive medication (30). Thus, in treated hypertensive patients, higher HBP readings could result from the insufficient duration of action of antihypertensive medication (31). More recent studies have identified a morning surge of BP that likely is resolved by the time a patient's OBP has been measured (32).

Some differences between OBP and out-of-office measurements may be due to the technology used to measure BP. In many studies and in most clinics, OBP is taken using a stethoscope and sphygmomanometer, whereas ABP and HBP are commonly monitored using electronic measuring devices. At least one study has used the same device in the clinic and at home and found that MH is still common (33).

Because hypertension is a continuous variable, the choice of a cut-off point for the diagnosis of hypertension is somewhat arbitrary. In one study (33), changing diagnostic cut-off points for OBP from 140/90 mmHg to 135/85 mmHg reduced the prevalence of MH by 50%. These data are consistent with the earlier observation that many patients with MH fall into the high normal range for OBP.

How can the new recommendation be applied?

The Canadian Hypertension Education Program has modified its 2006 recommendation on home/self BP monitoring (34). In addition to its other uses, the recommendation states that home/self monitoring (ie, HBP) should be considered in cases where BP is 'controlled in the office but not at home'.

Physicians should be aware of the possibility of MH and the increased risks associated with it. Attention must first be given to accurate and repeated BP measurements in the office, and these readings should be documented on more than one office visit. Good clinical judgment is also needed to determine the appropriateness of follow-up with ABP or HBP when MH may be present. MH may be suspected in those patients who have high normal BP associated with target organ damage, a strong family history of hypertension, multiple risk factors or levels of BP that fluctuate between hypertension and normotension. Cost, convenience and availability are important criteria in determining whether to measure either ABP or HBP. When using HBP to make the diagnosis, measurement on at least 15 different occasions is needed. Patients must use accurate, validated equipment and should be trained properly. Because therapeutic trials based on HBP and ABP are limited, physicians must use careful clinical judgment when making therapeutic decisions in patients with MH.

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