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To cite this article: Krzysztof Narkiewicz, Sverre E. Kjeldsen, Brent M. Egan, Reinhold Kreutz & Michel Burnier (2022) Masked hypertension in type 2 diabetes: never take normotension for granted and always assess out-of-office blood pressure, *Blood Pressure*, 31:1, 207-209, DOI: [10.1080/08037051.2022.2107483](https://doi.org/10.1080/08037051.2022.2107483)

To link to this article: <https://doi.org/10.1080/08037051.2022.2107483>



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Published online: 08 Aug 2022.



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Masked hypertension in type 2 diabetes: never take normotension for granted and always assess out-of-office blood pressure

Traditionally, the diagnosis of hypertension was based on office blood pressure (BP) measurements. BP status was defined as a binary: your patient was either normotensive or hypertensive. Introduction of ambulatory BP monitoring revealed that the picture is much more complex than we initially thought. Consequently, current European recommendations [1,2] recognise four BP categories: true normotension, sustained hypertension, white-coat hypertension and masked hypertension. The term ‘true normotension’ is used when both office and out-of-office measurements are concordant within normal limits, and ‘sustained hypertension’ is diagnosed when both values are elevated. White-coat hypertension refers to the untreated condition in which BP is elevated in the office, but is normal when assessed by ambulatory BP monitoring and/or home BP measurements. Conversely, masked hypertension is diagnosed in subjects whose BP is normal in the office, but is elevated on out-of-office measurements.

Even with carefully obtained office BP measurements, approximately 15–25% of individuals attending hypertension clinics have white-coat hypertension and 10–20% masked hypertension [2]. Prevalence of both BP phenotypes is affected by several factors including age [3–6]. While the concept of white coat hypertension is widely accepted by medical community, the relevance of masked hypertension is poorly recognised because it is more difficult to identify in clinical practice as general practitioners take no further steps when measured office BP values are normal. Nevertheless, there is growing evidence that this condition might be of special relevance in particular among patients with diabetes. Why should we pay more attention to detection and appropriate management of masked hypertension in diabetic patients?

First, the prevalence of masked hypertension in patients with diabetes is much higher than in the general population [7,8]. In a recent study published in *Blood Pressure*, masked hypertension was detected in 66% of the normotensive patients with diabetes referred to a tertiary centre in India [9]. In the population-based studies, the prevalence of masked hypertension is higher in younger subjects, smokers, and those with lower levels of physical activity, anxiety, and job stress [1,10]. Alcohol can increase masked hypertension, but that effect appears to be mediated mainly by effect on daytime BP and alcohol lowers night-time, i.e. alcohol does not impair dipping status [11,12]. Some of these factors

(smoking, alcohol abuse and stress) might contribute to masked hypertension in diabetics. However, patients with diabetes might represent distinctive ‘metabolically-driven’ phenotype of masked hypertension, and other mechanisms might be implicated. Obesity might play a profound role, as it has been shown to be associated with not only masked hypertension in untreated subjects [13,14], but also with masked uncontrolled hypertension in treated patients [15]. Elevated daytime BP might be related to low level of fitness with concomitant potentiated pressor response to exercise; high night-time BP might be a consequence of obesity and obstructive sleep apnoea frequently coexisting with diabetes. Other factors including chronic kidney disease, sodium and volume retention, and early vascular ageing might also impair buffering of BP response to routine activities and at the same time contribute to non-dipping BP pattern.

Second, the rate of incident sustained hypertension is significantly higher in adults with than without masked hypertension [16]. Patients with masked hypertension are prone to the early development of target organ damage [17,18]. Importantly, the risk of cardiovascular events is greater in masked hypertension in comparison to true normotension, and similar to that of sustained hypertension [19–21]. Masked hypertension in diabetes was found to have a significant association with left ventricular hypertrophy and albuminuria [7–9], and to increase the risk of cardiovascular and renal events, especially when BP elevations occur at night [21,22].

Thirdly, detection of masked hypertension should promptly lead to intensified management, especially of patients with diabetes. According to guidelines [1], factors contributing to the out-of-office BP elevation (overweight, smoking, alcohol abuse) should be discouraged and lifestyle interventions improving out-of-office BP should be implemented. The impact of antihypertensive treatment on cardiovascular outcomes in masked hypertension is unknown, and the first study addressing this issue is ongoing [23]. Despite limited data supporting improved outcomes by managing masked hypertension, based on the current evidence, pharmacotherapy should be considered to normalise the out-of-office BP during the day as well as during night-time.

Already a decade ago, Parati and Bilo [24] suggested that 24-h ambulatory BP monitoring should be performed in every patient with diabetes. Nocturnal hypertension and non-dipping pattern are the most prevalent manifestations of masked hypertension in diabetes [25]

limiting utility of traditional daytime home BP monitoring to detect this condition. However, recent technological development of electronic devices has enabled automated measurement of home BP during sleep with little if any interference with sleep quality [26]. These novel monitors are of particular relevance in patients with diabetes. Furthermore, the diagnosis and management of masked hypertension might be improved by introduction of cuffless BP devices. However, as stressed by a recent ESH statement [27], fundamental questions regarding their accuracy and implementation have to be carefully addressed before they can be recommended for clinical use.

What are the practical implications of these considerations? Diabetes *per se* is associated with a high cardiovascular risk. Screening for masked hypertension might help identifying patients at particularly elevated risk despite apparently normal office BP. European hypertension guidelines [1] include a special paragraph addressing general aspects of masked hypertension and stressing that this phenomenon is more prevalent in diabetes and in patients with chronic kidney diseases among whom a high percentage are suffering from diabetes. However, its relevance is not highlighted in the section or tables related to the management of hypertension in diabetes. Diabetes guidelines [28–30] recommend that all hypertensive patients with diabetes should monitor their BP at home, which might detect masked uncontrolled hypertension in treated patients. Unfortunately, these documents do not mention the relevance of masked hypertension in untreated patients with apparently normal office BP. There is a clear need to develop actions increasing awareness of masked hypertension among practicing physicians defining more precisely when and how to detect it. But at the same time, we should initiate new studies focussed on novel diagnostic methods and optimal treatments of this condition.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

The author(s) reported there is no funding associated with the work featured in this article.

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Received 20 July 2022; Revised 25 July 2022; Accepted 25 July 2022

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