Risk prediction by ambulatory blood pressure monitoring in non-diabetic and diabetic patients: better than office measurements

Giuseppe Mancia 1*, Rita Facchetti 1, and Guido Grassi1,2

1University Milano-Bicocca, Piazza dei Daini 4, 20126 Milan, Italy; and 2Clinica Medica, University Milano-Bicocca, Milan, Italy

This editorial refers to ‘Office measurement vs. ambulatory blood pressure monitoring: associations with mortality in patients with or without diabetes’, by M. Böhm et al., https://doi.org/10.1093/eurheartj/ehae337.

This issue of the European Heart Journal includes a study by Bohm and colleagues1 based on a large collection of ambulatory and office systolic blood pressure (SBP) data from Spanish clinical practice, which focuses on the relationship of ambulatory BP with cardiovascular and all-cause mortality in diabetic patients.1 The study shows firstly that, in diabetic patients, the risk of cardiovascular and all-cause mortality increases progressively and steeply from a 24 h mean SBP of <120 mmHg to an SBP > −160 mmHg, i.e. the SBP range in which most individuals from the population lay. Secondly, the authors show that at each ambulatory SBP level, the risk is clearly greater in diabetic than in non-diabetic patients. Thirdly, the steep increase in mortality with a 24-h SBP increase can also be seen when mean day-time and night-time SBP values are analysed separately. Fourthly it is shown that diabetes further increases the risk of mortality in phenotypes that can be identified by joint office and ambulatory BP measurements, such as true normotension (normal 24-h and office BP), masked hypertension (normal office and high 24-h BP), and sustained hypertension (high office and 24 h BP), with an apparent preservation of a greater mortality risk in the latter two hypertensive phenotypes compared with the normotensive phenotype. These findings considerably extend previous information on the epidemiological importance of ambulatory BP to stratify cardiovascular risk in diabetes, an issue which had in the past lagged behind that obtained in the general or non-diabetic population. The very large dimension of the database (~60 000 patients, of whom ~11 000 had diabetes) gives strength to the results.

However, the study also includes several findings that differ from current epidemiological data, suggesting that what is believed to be well established evidence may benefit from further discussion and research. One finding is that in the diabetic patients of the present study the risk of outcomes increased steeply with the progressive elevation of day-time SBP, with apparently no or only a minor difference in slope compared with the outcome increase associated with the night-time SBP elevation. This is not in line with the current concept that night-time SBP is a much better predictor of cardiovascular outcomes than day-time SBP,2 a concept that was supported several years ago also by the evidence that night-time BP selectively predicted the appearance of renal complications in patients with diabetes.3 This is to some extent challenged by the evidence of Boehm et al.,1 which rather favours the conclusion that in diabetes, day-time and night-time BP are similarly important for cardiovascular risk stratification. Whether this is specific for diabetes or extends to other conditions remains to be seen and, given its large dimension, this may be made possible by further analysis of the Spanish database. Another finding is that, in non-diabetic individuals, office SBP increases were not only less sensitive predictors of outcomes than ambulatory BP increases (a finding that is confirmatory of previous studies and meta-analyses),2 but they were almost not differentially predictive of outcomes over SBP values within the <120–159 mmHg range. This is in contrast to classical epidemiological data, which show that an increase in office SBP from ~110 mmHg to ~180 mmHg is associated with a clearcut progressive increase of cardiovascular outcomes, as exemplified by a meta-analysis of >60 population studies for a total of 1 million individuals, mostly non-diabetic.4 Indeed, the association of an increase of office SBP with cardiovascular outcomes is the basis of the BP classification into optimal, normal, high-normal, and grade 1, 2, and 3 hypertension adopted by hypertension guidelines at present6,5 and ambulatory BP increases were not only less sensitive predictors of outcomes than ambulatory BP increases (a finding that is confirmatory of previous studies and meta-analyses),2 but they were almost not differentially predictive of outcomes over SBP values within the <120–159 mmHg range. This is in contrast to classical epidemiological data, which show that an increase in office SBP from ~110 mmHg to ~180 mmHg is associated with a clearcut progressive increase of cardiovascular outcomes, as exemplified by a meta-analysis of >60 population studies for a total of 1 million individuals, mostly non-diabetic.4 Indeed, the association of an increase of office SBP with cardiovascular outcomes is the basis of the BP classification into optimal, normal, high-normal, and grade 1, 2, and 3 hypertension adopted by hypertension guidelines for the general population.6,5 It is also the basis, together with the results of outcome trials, for the current discussion on whether SBP should be lowered by treatment to <140, <130, or <120 mmHg, a discussion which would have no justification if there were little or no outcome differences at these office SBP values. Interestingly, Bohm and colleagues1 did show an increase of outcomes from 120 to 160 mmHg office SBP in diabetic patients, but the increase was quantitatively modest compared with what has been reported in large epidemiological studies such as the Multiple Risk Factor Intervention Trial,6 in which, compared with non-diabetic individuals, diabetic patients exhibited, as in the present study, an increase of mortality at...
each office SBP level. They further showed, however, a steep increase in the mortality risk from the lowest to the highest office SBP value. The low sensitivity of office SBP as a prognostic marker of outcomes in non-diabetic, and in part also in diabetic patients, can be difficult to explain, although an unbalanced number of cardiovascular risk factors between different office SBP groups or an office SBP misclassification due to limited standardization and accuracy of office BP measurements might be among the factors to examine. It should additionally be appreciated that an underestimation of office SBP-related prognostic value might have, as a consequence, an overestimation of the advantages of using ambulatory BP for risk stratification in the general hypertensive population, an issue that is currently under debate.

A third finding of Bohm and colleagues that differs from the evidence offered by the medical literature is the absence of a detrimental prognostic value of white coat hypertension, which in a few initial studies was described as clinically innocent but is now regarded by long-term studies and meta-analyses as prognostically adverse, although less so than what can be seen in sustained hypertension. Within the databases available in the literature, the white coat hypertension subgroup is of special clinical interest because of its high prevalence in the hypertensive population, i.e. in more than one out of three or one out of two hypertensive patients in the general and elderly hypertensive population, respectively. Bohm et al. show that in diabetes, white coat hypertension does not carry a greater risk of outcomes than in normotension, thereby aligning with the neutral outcome data reported for this condition by some earlier studies. The difference from the literature is particularly evident in non-diabetic white coat hypertensive patients in whom an outcome risk lower than that seen in normotensive patients is reported, albeit with a difference of uncertain statistical significance. This has some paradoxical aspects because in the last 20 years not only have several longitudinal studies shown an increased outcome risk in non-diabetic patients with white coat hypertension, but evidence has been obtained on the multiple factors that may account for this clinically unfavourable evidence. As recently reviewed, cross-sectionally, white coat hypertensive individuals (i) exhibit a dyslipidaemic, dysglycaemic, and dysuricaemic risk factor profile compared with normotensive individuals; (ii) although confined by definition to the normal range, their home and/or 24-h BP values are several mmHg higher than those measured in the normotensive phenotype; (iii) nocturnal hypertension, i.e. a condition characterized by a marked increase in the risk of fatal and non-fatal outcomes, has a prevalence that may be up to 30% greater than in normotensive individuals; (iv) sympathetic activity, as measured by nerve traffic recording to skeletal muscle circulation, is increased to levels similar to those of sustained hypertension; and (v) most importantly, individuals with white coat hypertension are characterized by a greater prevalence of subclinical damage of the heart, the kidney, the brain, as well as the small and large arteries, all associated with a high cardiovascular risk. To cite some examples, in a general population study the prevalence of echocardiographic left ventricular hypertrophy was almost four times as high in white coat and masked hypertension as in normotension, although remaining, in either condition, substantially lower than the prevalence seen in sustained hypertension. This is clinically relevant because left ventricular hypertrophy is known to be prognostically detrimental, a conclusion in line with the reduced survival of people with left ventricular hypertrophy from the same population. Furthermore, white coat hypertensive subjects had a significant 10-year increase in the risk of new-onset sustained hypertension, new-onset diabetes, and new-onset echocardiographic left ventricular hypertrophy compared with normotensive subjects. Finally in the white coat hypertension fraction of the general population, the risk of cardiovascular mortality over an 18-year follow-up was intermediate between subjects with in- and out-of-office normotension and those with in- and out-of-office hypertension. Thus, plenty of factors may account for an increased risk of mortality in white coat hypertension, and this has been directly shown in long-term longitudinal studies. Indeed, just a fraction of some of these factors can drive a risk increase because a greater risk of cardiovascular mortality has been recently detected in white coat hypertensive individuals in whom subjects with cardiac or renal subclinical damage had been excluded. To offset these detrimental influences and turn white coat hypertension into a prognostically neutral (or even prognostically favourable) condition compared with normotension, one would have to assume the existence of protective factors that at the moment appear difficult to imagine.

In conclusion, the study by Bohm et al. provides clear evidence on the superior ability of 24-h SBP to stratify the cardiovascular risk of diabetic patients compared with office SBP. It further shows that the increased ability of 24-h SBP to predict outcomes is shared by both the daytime and the night-time mean SBP values, separately considered. It finally shows that at each ambulatory BP level, diabetic patients exhibit a greater risk compared with non-diabetic patients. There are some results in the study that are not entirely in line with what is the current prevailing view on the BP–outcome relationship, such as the apparently similar prognostic value of day-time and night-time SBP, the overall prognostic insensitivity of office SBP, especially in non-diabetic patients, and the absence of an adverse prognostic effect of white coat hypertension. This will keep research on these issues alive and active, without detracting from the evidence on the crucial importance of collecting ambulatory BP data in patients with diabetes, whenever this is feasible.

**Declarations**

**Disclosure of Interest**

All authors declare no disclosure of interest for this contribution.

**References**


