Given the increase in prevalence of obesity, survival to older age, and urbanization, the projected global number of people with diabetes mellitus will double within decades (http://www.eatlas.idf.org/Prevalence). Physicians care for an ever-increasing load of elderly patients with diabetes mellitus. As a matter of fact, quality of care of patients with diabetes mellitus has become a measure of quality in internal medicine, and diabetes mellitus practice improvement modules are part of the American Board of Internal Medicine recertification program (http://www.abms.org/Maintenance_of_Certification). Recently it became clear that a major (and most reachable) intersection on the road to improving prognosis of patients with diabetes mellitus is the successful lowering of their blood pressure to levels well below those previously considered the goal for subjects without diabetes mellitus.

The vast body of research regarding blood pressure of patients with (as well as without) diabetes mellitus relies on office blood pressure measurements. However, it is now clear that 24-hour ambulatory blood pressure (ABP) monitoring provides data that are more closely linked to patients’ daily behavior. Compared with office blood pressure, the 24-hour ABP average may be closer to the individual’s “true” blood pressure. This is the basis for the overall stronger links of the latter with target organ damage, cardiovascular events, and, ultimately, survival.

Can we apply the vast knowledge generated from hypertensive and general populations with 24-hour ABP monitoring to patients with diabetes mellitus? Are 24-hour ABP monitoring patterns such as white coat effect, masked hypertension, nocturnal hypertension, and nondipping (the lack of the sleep-associated blood pressure or heart rate decline) represented in patients with diabetes mellitus as in the general hypertensive population? Surprisingly there are relatively few data to answer such questions. Nevertheless, there is good reason to suspect that some of the established patterns of 24-hour ABP, that there is some discordance between these cutoff definitions: a sizable minority (about 17%) with apparently normal 24-hour ABP have nocturnal hypertension. Subjects with diabetes mellitus are frequently nondippers, and at a given office blood pressure they have been shown to have increased odds for sleep hypertension and masked hypertension.

What are the mechanisms for the attenuated blood pressure decline during sleep in diabetes mellitus? The lack of definite answers to this question in part reflects our incomplete understanding of the sleep-associated dipping phenomenon, but we do have some clues. Subjects with diabetes mellitus may be more likely to have obesity-associated obstructive sleep apnea, a recognized cause for nondipping; orthostatic hypotension because of autonomic neuropathy might negate blood pressure changes induced by circadian and sleep-wake cycles; and diabetic nephropathy, heart failure, and perhaps a more general form of salt retention might dampen the blood pressure reductions expected during sleep-related sympathetic withdrawal.

Subjects with diabetes mellitus are also more prone to nocturia, because of osmotic diuresis, advanced nephropathy with concentrating defects, obstructive sleep apnea, urinary tract infections, neurogenic bladder, misuse of diuretics, heart failure with central compartmentalization of volume when supine, gastrointestinal motility disorders with delayed fluid absorption, and prostatic hypertrophy, which is common in these generally older patients. Nocturnal awakenings and getting out of bed to urinate elevate night blood pressure and heart rate to daytime levels, and when repeated may give appearance of nondipping if these measurements are captured and calculated within the night’s average. Notwithstanding issues of measurement, in subjects with diabetes mellitus, sleep is genuinely accompanied by a lesser decline of blood pressure, as observed during a relatively brief, uninterrupted, daytime sleep. This confirms that the roots of nondipping in diabetes mellitus lie beyond disturbed sleeping patterns.

In this issue of Hypertension, Palmas et al describe predictors of mortality in a large multiethnic cohort of elderly subjects with diabetes mellitus. They used 24-hour ABP monitoring and have several interesting findings. A surprising negative finding is that neither office nor ABP was independently related to mortality. This is difficult to comprehend,
because blood pressure differences of this magnitude are usually associated with mortality.\textsuperscript{8} There are several mutually inclusive explanations. First, in this cohort with multiple comorbidities and a mortality rate of 37 per 1000 patient-years, the possibility of reverse epidemiology and biphasic relationships between blood pressure and mortality, eg, J- or U-curve pattern, might have been overlooked. Second, multiple interrelations between measures of blood pressure, age, metabolic abnormalities, medications, and comorbidities might have confounded the serious effects of high blood pressure in a way that cannot be fully adjusted for. Indeed, removal of only one of these parameters from the model, urinary albumin:creatinine ratio, resulted in significant association between pulse pressure and mortality. It also could be that all-cause mortality represents an insensitive end point, and perhaps analysis of nonfatal cardiovascular events would have been more revealing.

Interestingly, the number of patients designated as having their blood pressure controlled was low at the office (32\%) and even lower by ABP (17\%). This finding of office masking of ambulatory hypertension, confirms our previous findings\textsuperscript{4} on the specific importance of masked hypertension in diabetes mellitus. Also, the very high prevalence of nondipping, \textasciitilde 70\%, points to its significance in diabetes mellitus, because it was indeed associated with predicting mortality in this and in other cohorts of patients with hypertension.\textsuperscript{9}

Another finding of Palmas \textit{et al}\textsuperscript{3} is the association with mortality, of not only office pulse rate, but also nondipping of pulse rate, recorded by 24-hour ABP monitoring. This may represent a variety of pathophysiologic processes: preferential parasympathetic denervation in the autonomic neuropathy of long-standing diabetes mellitus; heart failure; the increased sympathetic activity of chronic kidney disease; and obstructive sleep apnea, as well as nocturnal awakenings for a variety of reasons as discussed above. Indeed, nocturia in the elderly was found to be associated with mortality,\textsuperscript{10} especially in the presence of coronary disease.

The ambulatory arterial stiffness index derived from the regression of diastolic to systolic ABP, a promising although as-yet poorly understood arterial characteristic that is, however, readily available from 24-hour ABP, predicted mortality in this study. Interestingly, ambulatory arterial stiffness index was not a significant predictor once 24-hour pulse pressure was entered into the model, evidence for its representation of an arterial property, as well as a reminder that it may be artificially elevated in nondippers.\textsuperscript{11}

This important study re-emphasizes the importance of using 24-hour ABP monitoring if we want to reduce misclassification (masked hypertension) and be able to use the unique variables easily derived from 24-hour ABP monitoring, such as blood pressure and pulse rate nondipping, important for proper prognostication of this high-risk population.

Disclosures

None.

References


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