

# Data from the Dublin outcome study

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**Background** Ambulatory blood pressure monitoring (ABPM) has proven to be a superior predictor of cardiovascular events when compared with clinic or office blood pressure measurement (CBPM). The purpose of the Dublin Outcome Study was to evaluate the predictive value of various established and new ABPM indices in a large sample of patients referred for management of cardiovascular risk.

**Methods and results** At baseline 11 291 patients (5326 men, mean age 54.6 years), who were not on antihypertensive medication, underwent ABPM. Using all blood pressure readings from each individual, diastolic blood pressure was plotted against systolic blood pressure, and the regression slope was calculated. Ambulatory arterial stiffness index (AASI) was defined as one minus this regression slope. After a median follow-up of 5.3 years there were 566 cardiovascular deaths. In a Cox proportional-hazards model the unadjusted and adjusted (for other cardiovascular risk factors, mean arterial pressure and pulse pressure) hazard ratios for an abnormal AASI were 2.05 (95% confidence intervals;

1.60–2.63,  $P < 0.0001$ ) and 1.59 (1.23–2.04,  $P = 0.001$ ) respectively.

**Conclusions** ABPM is superior to clinic or office blood pressure measurement in predicting cardiovascular mortality AASI, which may be derived simply from ABPM, is a novel index in determining prognosis. *Blood Press Monit* 12:401–403 © 2007 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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## Introduction

Clinic or office blood pressure measurement (CBPM) has clearly demonstrated the relationship between blood pressure and cardiovascular risk. There are, however, numerous criticisms of CBPM, which include interobserver and intraobserver variability, and terminal digit preferences, all of which may bias the accuracy of measurement. Ambulatory blood pressure monitoring (ABPM) can overcome many of these deficiencies. We undertook the Dublin Outcome Study to ascertain the usefulness of ABPM in risk stratification in a large cohort of referred patients and to determine the additional predictive value of ABPM over and above CBPM. We also tested the predictive value of ambulatory arterial stiffness index (AASI) in this cohort.

## Methods

### Patient selection

A total of 11 292 patients with CBPM and ABPM data available from their initial visit when off treatment were entered into this prospective study. Patients were excluded if adjusting variables [sex, age, body mass index (BMI), smoking status, presence of diabetes mellitus, and history of cardiovascular disease] were not recorded.

### Ambulatory blood pressure measurement

ABPM measurements were made every half an hour throughout the 24-h period using Spacelabs 90202 and

90207 monitors (Spacelabs Inc., Redmond, Washington, USA; Spacelabs, Wokingham, Berkshire, UK) (3).

### Clinic blood pressure measurement

CBPM was measured by a nurse in the nondominant arm after 5 min of quiet sitting in accordance with contemporary recommendations using either a standard mercury sphygmomanometer or the Omron HEM-705CP (Omron Healthcare, Inc. Bannockburn, Illinois, USA).

### Derivation of ambulatory arterial stiffness index

Using all blood pressure readings from each individual, diastolic blood pressure (DBP) was plotted against systolic blood pressure (SBP), and the regression slope was calculated. AASI was defined as one minus this regression slope. AASI was dichotomized using the upper boundary of the 95th prediction interval in relation to age in Belgian, Chinese and Irish normotensive patients enrolled in the International Database of Ambulatory Blood Pressure Monitoring.

## Results

### Baseline characteristics

At enrolment, the 11 291 patients had a mean ( $\pm$  SD) age of  $54.6 \pm 14.6$  years (range, 16–96 years). AASI was higher ( $P < 0.001$ ) in women than men (0.42 vs. 0.40), in the presence as opposed to the absence of diabetes

**Table 1 Hazard ratios for mortality in relation to the ambulatory arterial stiffness index and pulse pressure [3]**

Cause (number) of death	AASI	Pulse pressure	Dichotomized AASI	Dichotomized pulse pressure
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Cardiovascular (n=566)				
Unadjusted	1.59 (1.47–1.71) <sup>  </sup>	1.66 (1.58–1.74) <sup>  </sup>	2.05 (1.60–2.63) <sup>  </sup>	2.81 (2.37–3.34) <sup>  </sup>
Adjusted <sup>a</sup>	1.14 (1.04–1.24) <sup>§</sup>	1.19 (1.09–1.30) <sup>  </sup>	1.71 (1.33–2.19) <sup>  </sup>	1.19 (0.98–1.44)
Fully adjusted <sup>b</sup>	1.08 (0.98–1.19)	1.16 (1.05–1.27) <sup>§</sup>	1.59 (1.23–2.04) <sup>  </sup>	1.11 (0.90–1.35)
Stroke (n=151)				
Unadjusted	1.71 (1.47–1.97) <sup>  </sup>	1.68 (1.52–1.84) <sup>  </sup>	3.06 (2.01–4.64) <sup>  </sup>	2.70 (1.95–3.76) <sup>  </sup>
Adjusted <sup>a</sup>	1.23 (1.04–1.45) <sup>‡</sup>	1.12 (0.94–1.32)	2.49 (1.64–3.80) <sup>  </sup>	0.99 (0.69–1.44)
Fully adjusted <sup>b</sup>	1.21 (1.01–1.45) <sup>‡</sup>	1.04 (0.87–1.25)	2.42 (1.58–3.72) <sup>  </sup>	0.87 (0.59–1.28)
Cardiac (n=358)				
Unadjusted	1.57 (1.42–1.73) <sup>  </sup>	1.66 (1.56–1.77) <sup>  </sup>	1.78 (1.29–2.47) <sup>  </sup>	3.04 (2.45–3.78) <sup>  </sup>
Adjusted <sup>a</sup>	1.11 (0.99–1.24)	1.22 (1.10–1.37) <sup>  </sup>	1.44 (1.03–2.00) <sup>‡</sup>	1.34 (1.05–1.71) <sup>‡</sup>
Fully adjusted <sup>b</sup>	1.03 (0.91–1.16)	1.21 (1.08–1.36) <sup>§</sup>	1.32 (0.94–1.84)	1.28 (0.99–1.65)

AASI, ambulatory arterial stiffness index; HR, hazard ratios (95% confidence intervals) associated with a 1 SD increase in AASI and pulse pressure or with an abnormal AASI or pulse pressure dichotomized based on the upper boundary of the 95% prediction interval for individual data in relation to age in a normotensive reference population. AASI and pulse pressure are expressed in dimensionless units and mmHg, respectively [3].

<sup>a</sup>Adjusted for sex, age, body mass index, smoking, diabetes mellitus, a history of cardiovascular disease, and mean arterial pressure.

<sup>b</sup>AASI additionally adjusted for pulse pressure and vice versa.

<sup>‡</sup> $P < 0.05$ , <sup>§</sup> $P < 0.01$ , <sup>||</sup> $P < 0.001$ .

mellitus (0.46 vs. 0.41) or a history of cardiovascular disease (0.47 vs. 0.41). The corresponding differences in pulse pressure (PP) (57.4 vs. 55.6 mmHg, 61.3 vs. 56.2 mmHg, and 59.6 vs. 56.1 mmHg) were also significant ( $P < 0.001$ ).

#### Clinic and ambulatory blood pressures as predictors of mortality risk [1]

ABPM predicted cardiovascular mortality over and beyond systolic CBPM ( $P < 0.001$ ). The hazard ratios (HRs) associated with a 10 mmHg increase in systolic ABPM were 1.19 (95% CI, 1.13–1.27;  $P < 0.001$ ), 1.12 (95% CI, 1.06–1.19;  $P < 0.001$ ) and 1.21 (95% CI, 1.16–1.28;  $P < 0.001$ ) for daytime, nighttime 24-h measurements respectively. The corresponding adjusted HRs associated with a 5 mmHg increase in DBP were 1.09 (95% CI, 1.02–1.11;  $P < 0.01$ ), 1.03 (95% CI, 0.99–1.07;  $P = \text{NS}$ ) and 1.09 (95% CI, 1.04–1.13;  $P < 0.05$ ) respectively.

#### Ambulatory arterial stiffness index and pulse pressure as predictors of cardiovascular mortality [2]

In unadjusted Cox regression the HRs for total cardiovascular mortality, and also for cardiac and stroke mortality, associated with both indices of arterial stiffness, analysed as continuous variables, were highly significant. With adjustments applied for baseline covariates, both AASI and PP continued to predict total cardiovascular mortality. After application of these adjustments, AASI, but not PP, also predicted fatal stroke (mutually adjusted HRs for one SD increase, 1.21 vs. 1.04;  $P = 0.02$  vs. 0.66), whereas PP predicted only cardiac mortality (HRs, 1.03 vs. 1.21;  $P = 0.63$  vs. 0.002). When AASI was analysed as a dichotomous variable, both without and with the same adjustments as before, elevated values of AASI were significantly and independently associated with the

higher mortality from cardiovascular, cerebrovascular and cardiac disease (Table 1).

#### Discussion

To our knowledge, this study is one of the largest to look at ABPM and cardiovascular mortality risk in a western adult hypertensive population including the elderly, who were not on antihypertensive medication at the time of blood pressure measurement. We have shown that after adjustment for CBPM, ABPM provides additive prognostic power [1,3] and that this is particularly true for patients with elevated nighttime pressures.

AASI, a new index easily derived from ABPM, is based on the concept that the relationship between systolic and diastolic blood pressure varies during the day and that this relation largely depends on the structural and functional characteristics of the large arteries. Systolic and diastolic blood pressure increase proportionally in normal individuals with elastic arteries. In contrast, in patients with stiffer arteries, for any given increase in systolic pressure, diastolic pressure will increase less or even decrease compared with the normal situation. Hypertension accelerates arterial stiffening and leads to vascular remodelling. In the early stages of hypertension, at lower levels of blood pressure, arterial stiffness might depend more on the functional properties of the large arteries rather than on advanced structural damage. This might explain why AASI was more predictive in participants with ambulatory normotension [2].

The Dublin Outcome Study demonstrates that ABPM is superior to CBPM in risk stratification in a high-risk cardiovascular population, and that AASI, which is easily derived from ABPM, offers new

insights into arterial stiffness. Taken collectively these characteristics of ABPM add to the growing evidence that the technique should be readily available in clinical practice.

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