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Comparison of Usefulness of Systolic, Diastolic, and Mean Blood Pressure and Pulse Pressure as Predictors of Cardiovascular Death in Patients ≥ 60 Years of Age (The Dubbo Study)

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Blood pressure (BP) is an important predictor of future cardiovascular risk. Clinicians have traditionally recognized the importance of systolic BP, especially in older adults.¹ BP is also characterized by its pulsatile (estimated by pulse pressure [PP]) and steady (estimated by mean arterial pressure) components.² Two recent studies^{3,4} have emphasized the importance of PP, defined as systolic BP minus diastolic BP, as a predictor of cardiovascular events or mortality in the elderly. Another study⁵ highlighted mean BP, defined as 1/3 systolic BP plus 2/3 diastolic BP, as a predictor of cardiovascular disease risk. Data from the Framingham Heart Study⁶ and other studies⁷ indicate that systolic BP increases continuously with age, whereas diastolic BP increases until age 60 years and then begins to decrease steadily. As a result, PP may become a more important BP measurement associated with cardiovascular disease in older persons.⁸ Darne et al² were among the first to report that PP, in addition to mean BP, was an independent cardiovascular risk factor. Mean BP has not been as extensively studied, with positive associations with cardiovascular disease in some^{5,9,10} but not all¹¹ studies. It remains unclear which measures of BP, either alone or in combination, best predict the risk of cardiovascular disease mortality. Therefore, we studied the use of systolic BP, diastolic BP, PP, and mean BP in an elderly cohort of men and women aged ≥ 60 years at baseline with no history of cardiovascular disease. Using BP values at baseline, we compared the associations of each BP measure with the risk of cardiovascular disease mortality prospectively over 12 to 13 years of follow-up.

The Dubbo Study is an ongoing prospective study in an elderly Australian cohort first examined in 1988.¹² All noninstitutionalized residents of the semi-urban town of Dubbo, New South Wales, born before 1930 were eligible; the participation rate was 73%, with an ultimate cohort of 2,805 men and women. Methods and measures have already been described in detail.¹² Briefly, the baseline examinations consisted of demographic, psychosocial, and standard cardiovascular risk assessment. Two BP readings were obtained after 10 minutes of seated rest, using phase V as diastolic. The second of these 2 readings was used in the present analyses. The study was approved and reapproved by institutional ethics committees at St. Vincent's Hospital Sydney, the University of New South Wales (Sydney, Australia), and the Australian National University (Canberra, Australia). All participants gave written informed consent.

Outcomes until September 2001 are included in the present analysis. Hospitalization and death records were monitored continuously, and postal surveys were conducted every 2 years to confirm vital status. The most recent survey successfully traced >95% of the surviving participants. Records were coded according to the *International Classification of Disease*, 9th and 10th editions (ICD-9 and ICD-10).

We excluded participants with prior coronary artery disease ($n = 426$), those lost during the follow-up period ($n = 52$), and those with missing values for diastolic pressure ($n = 1$). Multivariate analyses using Cox proportional-hazards models were performed using SPSS for Windows, Release 9.0 (SPSS Inc., Chicago, Illinois). The outcome was cardiovascular death, defined as death due to coronary artery disease or stroke, ICD-9 codes (410 to 414.9, 427, and 430 to 436.9), and ICD-10 codes (I20 to I25, I46, I60 to I67.9, and G45). Diabetes mellitus was identified from plasma glucose levels, history of diabetes, or therapy.¹³ Patients who did not meet these criteria were coded as “nondiabetic”. Additionally, ex-smokers were coded as nonsmokers. Analyses were stratified by hypertension treatment status and gender. The assumption of proportional hazards was confirmed in all models.

Table 1 lists baseline risk factors in subjects according to hypertension treatment status. In this population-based sample, after exclusions, 43% had treated hypertension.

In subjects who did not receive hypertension treatment, Tables 2 and 3 list hazard ratios, 95% confidence intervals, and p values for each BP measure, along with model-fit statistics. In models adjusting for age, diabetes mellitus, education, smoking status, total cholesterol, and body mass index, all BP measures were directly associated with the risk of cardiovascular death. Systolic pressure and mean BP appear to be the best predictors among the 4 BP measures. In women (Table 2), mean BP was a slightly better predictor than systolic BP, and in men (Table 3), systolic BP was a slightly better predictor than mean BP. Models with any 2 BP parameters yielded identical -2 log likelihoods because of the linear relation between BP variables. The addition of diastolic BP, PP, or mean BP to the model with systolic BP did not improve the model fit (models 4 to 7) appreciably compared with the model with systolic BP alone (model 1).

For subjects taking hypertension medication, systolic BP, diastolic BP, PP, and mean BP were tested, and none of these measures were a significant predictor of cardiovascular disease death. The coefficients for a 1-SD change in systolic BP, diastolic BP, PP, and mean BP were associated with p values of 0.1, 0.1, 0.5, and 0.1 in women, and 0.5, 0.4, 0.8, and 0.4 in men, respectively.

In this population-based study, all 4 BP measures alone were directly associated with the risk of cardiovascular disease mortality in subjects not taking hypertension medications. Of the 4 measures, both systolic BP and mean BP were the best predictors. Given the relative ease of calculation, systolic BP is a clinically superior measure to mean BP.

This population-based study included a more representative sample than those recruited for clinical trials.^{4,5,14} Also, previous studies^{8,15,16} compared 10 mm Hg changes in BP for each measure, whereas we compared BP measures by a 1-SD change in each respective measure to account for the different distributions¹⁷ (Table 1). Other studies^{4,5} do not directly compare PP with standard BP measures. Our data show that PP is as good a predictor as previously reported,¹⁷ but when compared with systolic BP, it is slightly inferior.

Few studies^{5,9,10,18} have prospectively addressed the effect of mean BP in relation to cardiovascular disease. Dyer et al¹⁰ found that the steady component of BP (highly correlated with mean arterial pressure) was more strongly associated with cardiovascular disease risk than PP in 4 Chicago epidemiologic studies. Among subjects with a history of

myocardial infarction, 1 study indicated a significant 12% increase in recurrent myocardial infarction for each 10-mm Hg increase in mean BP.¹⁸ However, mean BP was a weaker predictor than PP and was not associated with cardiovascular mortality. We found that mean BP may be strongly associated with cardiovascular disease mortality, with a hazard ratio of 1.4 for cardiovascular death for a 1-SD (21.8 mm Hg) increase in mean BP in women, and a hazard ratio of 1.3 in men.

There were significant interactions between BP measures and gender and hypertensive medication use; therefore, analyses were stratified on this basis. Previous studies including women have controlled for gender,¹⁷ as opposed to stratifying analyses. Our results indicated that it may be useful to examine the effects separately by gender, because there appear to be significant differences. We also found that BP measures were significant predictors only in those not receiving hypertensive treatment. This is also consistent with previous evidence,¹⁶ and it may be useful to stratify on this basis in the future.

Findings from The Dubbo Study are similar to those reported by some other cohorts of older adults. The Cardiovascular Health Study (CHS) also found that systolic BP was the best predictor of cardiovascular events¹⁷ when compared with diastolic BP and PP. The Hypertension Detection and Follow-up Program (HDFP) findings demonstrate that the predictive power of PP was similar to that of systolic BP.¹⁹ The Multiple Risk Factor Intervention Trial (MRFIT), although not specifically in the elderly, recently confirmed that systolic and diastolic BPs are better predictors of cardiovascular disease-related mortality than PP.²⁰ These studies did not examine mean BP, which along with systolic BP was a good predictor in our study.

Any clinical advantage for using mean BP, which is a function of systolic and diastolic BPs, to evaluate cardiovascular disease risk remains unclear. In this regard, mean BP, when used in combination with other BP parameters, offers no additional ability to predict the risk of cardiovascular disease. However, in models with single BP parameters, mean BP was a slightly stronger predictor of cardiovascular disease death than systolic BP in women based on -2 log likelihoods. Therefore, either mean or systolic BPs may best predict the risk of cardiovascular disease when individual BP parameters are considered.

Clinicians are familiar with systolic BP as a risk factor. PP and mean BP are not often used clinically. To become useful clinically or to form part of future guidelines for the definition or treatment of high BP, PP and mean BP would have to be clearly superior to the traditional measures of systolic or diastolic BPs. Data from this population-based cohort study suggest that these are not clearly superior, and that there is no need to revise clinical or guideline approaches to the definition of hypertension in older adults.

In summary, all measures of BP were strongly and directly related to the risk of cardiovascular death, but systolic BP was the best single predictor in untreated subjects.

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TABLE 1

Means $\pm$ SE and Proportions (%) of Covariates by Hypertension Treatment Status and Gender in The Dubbo Study

	Untreated		Treated Hypertensives	
	Women (n = 708)	Men (n = 619)	Women (n = 631)	Men (n = 368)
Age (yrs)	67.9 $\pm$ 6.9	67.4 $\pm$ 6.4	70.6 $\pm$ 7.2	69.7 $\pm$ 6.9
Education (yrs)	10.4 $\pm$ 1.6	10.3 $\pm$ 2.0	10.0 $\pm$ 1.7	10.0 $\pm$ 1.9
BMI (kg/m ²)	25.0 $\pm$ 4.1	25.7 $\pm$ 3.5	26.7 $\pm$ 4.9	26.9 $\pm$ 4.0
Total cholesterol				
mmol/L	6.8 $\pm$ 1.2	6.2 $\pm$ 1.2	6.8 $\pm$ 1.3	6.1 $\pm$ 1.2
mg/dl	263 $\pm$ 46	240 $\pm$ 46	263 $\pm$ 50	236 $\pm$ 46
Systolic BP (mm Hg)	143 $\pm$ 25	142 $\pm$ 21	154 $\pm$ 24	151 $\pm$ 24
Diastolic BP (mm Hg)	77 $\pm$ 11	80 $\pm$ 12	80 $\pm$ 12	82 $\pm$ 12
PP	66 $\pm$ 22	62 $\pm$ 18	74 $\pm$ 21	68 $\pm$ 20
Mean arterial pressure	98 $\pm$ 14	100 $\pm$ 13	103 $\pm$ 14	104 $\pm$ 14
Smoker	12.5%	24.0%	10.5%	13.4%
Diabetes mellitus	3.6%	6.9%	9.1%	12.8%

BMI = body mass index.

TABLE 2

Cox Proportional-hazards Models for Cardiovascular Death in Women

	Model 1 Systolic BP	Model 2 Diastolic BP	Model 3 PP	Model 4 Mean BP	Model 5 Systolic BP & Diastolic BP	Model 6 Systolic BP & PP	Model 7 Systolic BP & Mean BP
Systolic BP	1.4 (1.1–1.7) 0.007				1.3 (1.0–1.6) 0.078	1.9 (1.1–3.2) 0.017	1.0 (0.6–1.7) 0.924
Diastolic BP		1.3 (1.1–1.7) 0.015			1.2 (0.9–1.6) 0.175		
PP			1.2 (1.0–1.5) 0.071			0.7 (0.4–1.2) 0.175	
Mean BP				1.4 (1.1–1.8) 0.002			1.4 (0.9–2.3) 0.175
–2 log likelihood	681	682	685	679	679	679	679

The table shows the hazard ratio (95% confidence interval) and p value for a 1-SD change in each BP measure. All models were adjusted for age, education, smoking, diabetes mellitus, total cholesterol, and body mass index.

TABLE 3

Cox Proportional-hazards Models for Cardiovascular Death in Men

	Model 1 Systolic BP	Model 2 Diastolic BP	Model 3 PP	Model 4 Mean BP	Model 5 Systolic BP & Diastolic BP	Model 6 Systolic BP & PP	Model 7 Systolic BP & Mean BP
Systolic BP	1.4 (1.1–1.8) 0.002				1.4 (1.1–1.9) 0.007	1.4 (1.0–2.1) 0.054	1.4 (0.9–2.2) 0.088
Diastolic BP		1.2 (1.0–1.4) 0.103			1.0 (0.8–1.3) 0.978		
PP			1.3 (1.1–1.6) 0.013			1.0 (0.7–1.4) 0.978	
Mean BP				1.3 (1.1–1.6) 0.009			1.0 (0.7–1.5) 0.978
–2 log likelihood	865	872	869	868	865	865	865

The table shows the hazard ratio (95% confidence interval) and p-value for a 1-SD change in each BP measure. All models were adjusted for age, education, smoking, diabetes mellitus, total cholesterol, and body mass index.