Tissue Doppler E prime velocity and E/E prime predict 19-year cardiovascular mortality in hypertension

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Background: We have previously shown that tissue Doppler assessments of left ventricular (LV) diastolic function predict cardiac events in a hypertensive population over a period of 4 years (1). These out-performed traditional echocardiographic measures in a well-treated hypertensive population.

Purpose: We aimed to test whether tissue Doppler assessment of LV diastolic function would predict cardiovascular (CV) mortality in the Hypertension Associated Cardiovascular Disease sub-study of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT).

Methods: ASCOT was a multicentre randomised trial with a 2x2 factorial design (2). Inclusion criteria for the study included hypertension and three other CV risk factors, including male sex and age over 55. Protocols, including for echocardiography, have been detailed previously (2, 3).

This study comprised the 519 patients recruited to the St Mary's Hospital site of the ASCOT study, who were followed for 19 years with mortality flagged by the Office for National Statistics. We have used all reported deaths on or before 31st January 2019. CV deaths include deaths due to coronary heart disease (CHD), stroke and other CV causes.

Echocardiography was performed one year after blood pressure control. mean tissue Doppler E' was calculated as the average of septal, lateral and inferior wall measurements over three cycles. The ratio of the transmitral Doppler E wave velocity and the composite mean of E' was used to calculate E/E' ratio.

Statistical analysis was performed using Python including multivariable Cox proportional hazards regression. A two-sided P-value <0.05 was considered statistically significant.

Results: After a median of 19 years, 317 patients survived (mean age at baseline 60.7y, 38 female) and 202 did not (mean age 68.1y, 30 female). Twenty-three deaths were due to CHD, 11 were due to stroke, 27 were due to other CV causes, and 76 were due to cancer. Baseline characteristics were not significantly different between those who survived to follow up and those who did not.

Unadjusted analysis showed a strong association between CV mortality and E' (HR=0.74, $p<0.005$) and E/E' (HR=1.18, $p<0.005$) (Table 1). The association between CV mortality and E' was attenuated slightly but persisted after adjusting for age and sex (HR=0.83, p=0.02) and after adjusting for age, sex and systolic BP (HR=0.83, p=0.03).

The association between CV mortality and E/E' was attenuated but persisted after adjusting for age and sex (HR=1.12, p=0.01) and after adjusting for age, sex and systolic BP (HR=1.11, p=0.04).

There was a weak association between all-cause mortality and both E/E' and E', which was null after adjusting for age and sex. Figure 1 shows unadjusted Kaplan Meier survival curves for E'.

Conclusions: Tissue Doppler E' velocity and E/E' predicted 19-year cardiovascular mortality in a hypertensive population independent of age, sex and systolic blood pressure.

Table 1: Multivariate analysis: hazard ratios for mean tissue Doppler E' velocity and mean tissue Doppler E/E'

		Model	Adjusted	Hazard ratio	Confidence interval	*p*-value
E'	Cardiovascular causes	Unadjusted		0.74	0.63-0.86	<0.005
		1	Age, sex	0.83	0.71-0.91	0.02
		2	Age, sex, systolic BP	0.83	0.71-0.98	0.03
	All causes	Unadjusted		0.86	0.80-0.94	<0.005
		1	Age, sex	0.98	0.68-1.54	0.64
		2	Age, sex, systolic BP	0.98	0.91-1.07	0.70
E/E'	Cardiovascular causes	Unadjusted		1.18	1.09-1.29	<0.005
		1	Age, sex	1.12	1.02-1.22	0.01
		2	Age, sex, systolic BP	1.11	1.00-1.22	0.04
	All causes	Unadjusted		1.06	1.00-1.13	0.04
		1	Age, sex	1.00	0.94-1.06	0.95
		2	Age, sex, systolic BP	0.98	0.92-1.04	0.53

Figure 1: Kaplan-Meier survival curves for mean tissue Doppler E' velocity (unadjusted)