HYPERTENSION

Age-specificity of blood-pressure-associated complications

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In an analysis of electronic health records, 1.25 million patients aged ≥30 years without diagnosed cardiovascular disease experienced 83,098 cardiovascular events during follow-up (median 5.2 years). Associations between incident cardiovascular disease and blood pressure differed for systolic and diastolic blood pressures and between the 12 cardiovascular end points examined.

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The concept that the risk associated with elevated systolic and diastolic blood pressure is age-specific and not concordant for all cardiovascular complications is not new, but has never before been highlighted on the scale of a new analysis by Rapsomaniki *et al.*[1] Compared with diastolic blood pressure, high systolic blood pressure had a greater effect on angina, myocardial infarction, and peripheral artery disease, whereas raised diastolic blood pressure had a greater effect on abdominal aortic aneurysm.[1] The Framingham investigators[2,3] and others[4] showed as early as 1971[2] that diastolic blood pressure was the strongest predictor of cardiovascular outcome in individuals aged <50 years, with an increasing importance of systolic blood pressure with older age. In 2001, Franklin *et al.* observed that with increasing age, predictors of coronary heart disease gradually shifted from diastolic to systolic blood pressure and then to pulse pressure.[3] Diastolic blood pressure was the strongest predictor of coronary heart disease in individuals aged <50 years.[3] In those aged 50–59 years, a transition occurred, during which all three blood-pressure indices were similarly accurate predictors, but in those aged ≥60 years, diastolic blood pressure was negatively associated with the risk of coronary heart disease, so that pulse pressure became a superior predictor to systolic blood pressure.[3] These epidemiological observations contradicted the long-held view, which guided the design of the first antihypertensive-drug trials, that diastolic blood pressure might be the best predictor of risk, being a measure of the resistance that the heart must overcome to eject blood.

Major limitations of the study by Rapsomaniki *et al.*[1] are that the analysis is entirely based on office blood pressure, which is no longer the state-of-the-art method to measure blood pressure or diagnose and manage hypertension;[5] includes no information about the quality of the office blood-pressure measurements across 225 primary care practices; and that information on the technique of blood-pressure measurement is also lacking.[1] The auscultatory approach can be used to measure systolic and diastolic blood pressure, whereas automated oscillometric devices extrapolate systolic and diastolic blood pressure from the measurement of mean arterial pressure. Digit and number preference provide information on the quality of auscultatory blood-pressure readings.[6] Diastolic and mean arterial pressures are similar throughout the arterial bed, whereas systolic blood pressure and pulse pressure are subject to systolic augmentation when the forward and reflected pressure waves collide in the central elastic arteries, a phenomenon that substantially increases with ageing.[6] Central systolic augmentation is a risk factor for stroke and myocardial infarction. To what extent the technique of office blood-pressure measurement and systolic augmentation[6] influenced findings is unknown.

Another major limitation is that lifetime risks were estimated by extrapolation of event rates recorded in individuals entering the cohort at different ages, rather than by following up each individual over his or her lifetime. On its own, this design aspect explains at least part of the heterogeneity with age in the associations between systolic and diastolic blood pressure and the 12 cardiovascular end points studied. Indeed, death of participants from stroke or myocardial infarction in middle age biases the analyses to the discovery of associations with other complications during older age. The difference in lifetime risk between individuals who were normotensive and those who were hypertensive at the index age of 30 years ranged from 0.1% for abdominal aortic aneurysm to 4.0% for stable angina.[1] The corresponding number of life-years lost ranged from 0.04 to 1.11 years, respectively. The risk differences were not adjusted, whereas the numbers of life-years lost were adjusted for sex, tobacco smoking, diabetes mellitus, and levels of total and HDL cholesterol.[1] The effect of differences in BMI between individuals who were normotensive and those who were hypertensive on the reported estimates is uncertain. In addition, adjustment for total-cholesterol and HDL-cholesterol levels is questionable, because these variables were not measured in 80% and 84% of the individuals, respectively.[1] The same uncertainty applies to the sensitivity analysis that included 679,354 individuals with unknown blood pressure at baseline.

The observed heterogeneity in the association between cardiovascular complications and systolic and diastolic blood pressures needs to be confirmed using out-of-office blood-pressure measurement.[1] We investigated the risk associated with systolic and diastolic blood pressure, using 24-h ambulatory monitoring as the state-of-the-art approach in 8,341 untreated individuals (mean age 50.8 years; 46.6% women; Table 1).[7] Isolated diastolic hypertension (pressure ≥80 mmHg) did not increase the risk of all-cause mortality, cardiovascular mortality, or stroke, but was associated with an increased risk of fatal or nonfatal cardiovascular, cardiac, or coronary events.[7] Isolated systolic hypertension (pressure ≥130 mmHg) and mixed diastolic plus systolic hypertension were associated with increased risks of all the aforementioned end points.[7] In individuals aged <50 years, 24-h diastolic blood pressure was the main driver of risk, reaching significance for total and cardiovascular mortality, and for all cardiovascular end points when combined with a nonsignificant contribution

Table 1 | Multivariable-adjusted standardized hazard ratios for 24-h systolic and diastolic blood pressures by age group[7]

End point	Adjustment	Age <50 years (n = 3,761)			Age ≥50 years (n = 4,580)		
		Number of events	Diastolic pressure HR (95% CI)	Systolic pressure HR (95% CI)	Number of events	Diastolic pressure HR (95% CI)	Systolic pressure HR (95% CI)
Mortality							
All-cause	A	64	1.38 (1.08–1.77)*	1.20 (0.86–1.66)	863	1.17 (1.10–1.25)‡	1.21 (1.14–1.29)‡
	FA		2.05 (1.26–3.33)*	0.56 (0.30–1.05)		1.03 (0.94–1.13)	1.19 (1.08–1.30)‡
Cardiovascular	A	16	2.34 (1.61–3.39)‡	2.23 (1.32–3.78)*	340	1.31 (1.18–1.44)‡	1.47 (1.35–1.61)‡
	FA		4.07 (1.60–10.40)*	0.44 (0.13–1.56)		0.96 (0.85–1.10)	1.51 (1.34–1.70)‡
Noncardiovascular	A	46	1.13 (0.83–1.55)	0.93 (0.61–1.42)	502	1.06 (0.97–1.16)	1.03 (0.94–1.12)
	FA		1.73 (0.96–3.12)	0.53 (0.25–1.13)		1.09 (0.95–1.25)	0.96 (0.84–1.10)
Fatal and nonfatal events							
All cardiovascular	A	47	1.65 (1.27–2.14)‡	1.68 (1.19–2.36)*	697	1.36 (1.27–1.46)‡	1.44 (1.35–1.53)‡
	FA		1.74 (1.03–2.93)§	0.92 (0.47–1.81)		1.06 (0.97–1.17)	1.39 (1.27–1.51)‡
Cardiac	A	37	1.53 (1.12–2.08)*	1.67 (1.07–2.62)§	440	1.25 (1.13–1.38)‡	1.37 (1.26–1.48)‡
	FA		1.67 (0.92–3.03)	0.88 (0.40–1.90)		1.01 (0.90–1.14)	1.36 (1.22–1.52)‡
Coronary	A	28	1.63 (1.16–2.30)*	1.67 (1.07–2.62)§	320	1.25 (1.13–1.38)‡	1.35 (1.23–1.48)‡
	FA		1.73 (0.87–3.45)	0.92 (0.37–2.24)		1.01 (0.88–1.15)	1.35 (1.18–1.53)‡
Stroke	A	7	2.31 (1.25–4.27)*	2.43 (1.12–5.26)§	249	1.61 (1.43–1.81)‡	1.65 (1.49–1.83)‡
	FA		2.24 (0.62–8.20)	1.04 (0.21–5.26)		1.14 (0.97–1.34)	1.52 (1.32–1.76)‡

The cause of death was unknown in 23 patients. Hazard ratios express the risk associated with an increase by one standard deviation in 24-h systolic (13.5 mmHg) or diastolic (8.2 mmHg) blood pressure. All models were adjusted for cohort, sex, age, BMI, tobacco smoking, alcohol consumption, serum cholesterol, and history of cardiovascular disease and diabetes mellitus. Adjusted models (A) include either systolic or diastolic blood pressure, whereas fully adjusted models (FA) include both systolic and diastolic blood pressures in addition to the aforementioned covariables. Significance of the hazard ratios: *$P \leq 0.01$, ‡$P \leq 0.001$, §$P \leq 0.05$. The interaction between blood pressure and age (continuous) in fully adjusted models was significant or borderline significant for cardiovascular mortality ($0.036 \leq P \leq 0.058$), all cardiovascular events ($0.0037 \leq P \leq 0.0048$), and coronary events ($0.012 \leq P \leq 0.043$). Reprinted from Li, Y. *et al.* Ambulatory hypertension subtypes and 24-hour systolic and diastolic blood pressure as distinct outcome predictors in 8341 untreated people recruited from 12 populations. *Circulation* doi:10.1161/CIRCULATIONAHA.113.004876.

of the 24-h systolic blood pressure.[7] In individuals aged >50 years, the 24-h systolic blood pressure predicted all end points, with a nonsignificant contribution of the 24-h diastolic blood pressure.[7] The interactions between age and the 24-h systolic and diastolic blood pressures reached significance for all cardiovascular and coronary events.[7]

Investigators in the Global Burden of Disease Study 2010[8] reported that high blood pressure is the leading risk factor for the global disease burden, and is estimated to cause 9.4 million deaths every year—more than half of the estimated 17 million deaths per year caused by cardiovascular disease. Rapsomaniki *et al.* emphasize the unmet need of improved implementation of existing blood-pressure-lowering strategies and management of other cardiovascular risk factors.[1] The suggestion from Peter Sever[9] to abandon diastolic pressure measurement and rely only on systolic pressure measurement for the management of hypertension is certainly not an option. Increasing awareness and education of patients and caregivers is probably the most-important step to take. In the study by Rapsomaniki *et al.*, only 80% of the 545,816 patients with hypertension had a systolic pressure <140 mmHg and a diastolic pressure <90 mmHg, and only 49% of these patients were treated.[1] The percentage of treated patients with controlled blood pressure was not reported. The situation in the UK is similar to that in other parts of the world. According to statistics generated by the International Collaborative Study of Cardiovascular Disease in Asia[10] performed in 2000–2001, 27.2% of the adult Chinese population aged 35–74 years had hypertension according to conventional blood-pressure measurement (totalling 129,824,000 patients). Among these individuals with hypertension, only 44.7% were aware of their high blood pressure, 28.2% were taking antihypertensive medication, and 8.1% of patients achieved blood-pressure control.[10]

In conclusion, the main message from the high-powered study by Rapsomaniki *et al.*,[1] and numerous other reports,[2–4,7] is that both systolic and diastolic pressures confer risk, and that their role as risk indicators changes with age. In our effort to curb the epidemic of noncommunicable diseases,[8] we must raise the pressure on hypertension, with the goal of extending life with disease-free years.

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Competing interests
The author declares no competing interests.

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