Left ventricular mass in relation to midlife blood pressure

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This editorial refers to 'Midlife blood pressure change and left ventricular mass and remodelling in older age in the 1946 British Birth Cohort Study², by A.K. Ghosh et al. on page 3287.

The 1946 Medical Research Council National Survey of Health and Development (MRC-NSHD) is the longest running birth cohort in the UK. Making use of this unique resource, Ghosh and colleagues have now demonstrated that left ventricular mass index (LVMI) and relative wall thickness at age 60–64 were associated with blood pressure (BP) or use of antihypertensive drugs from 36 years of age onwards, independent of current BP or treatment status.¹ Moreover, the rate of BP increase over time rather than the absolute BP level at a given age determined the LVMI at 60–64 years.¹ Ghosh and colleagues have to be congratulated for their meticulous analysis of longitudinal data spanning 28 years. Nevertheless, several issues cannot be disregarded in the interpretation of the results. First, as in all longitudinal studies, the attrition rate was high. Of 5362 initially enrolled participants, only 2856 were invited for echocardiography from 2006 onwards, independent of current BP or treatment status.¹ Moreover, the rate of BP increase over time rather than the absolute BP level at a given age determined the LVMI at 60–64 years.¹ Ghosh and colleagues have to be congratulated for their meticulous analysis of longitudinal data spanning 28 years. Nevertheless, several issues cannot be disregarded in the interpretation of the results. First, as in all longitudinal studies, the attrition rate was high. Of 5362 initially enrolled participants, only 2856 were invited for echocardiography from 2006 until 2011. Invitations were not sent to those who had died (n = 778), were living abroad (n = 570), had previously withdrawn from the study (n = 594), or had been lost to follow-up (n = 564). Of those invited, 539 (18.9%) accepted to be visited at home, but only 1653 (57.8%) underwent echocardiography and 1480 (51.8%) had analysable images. The authors argued that participants who opted for a home visit had higher BP and were less healthy, and that exclusion of this unhealthy group might have weakened the observed associations between left ventricular structure and BP. While this speculation might be true, it disregarded that half of the cohort was lost between 1946 and the time of invitation for echocardiography.

A second major issue was that at age 36 and 43, the Hawksley Random Zero sphygmomanometer was used, while an Omron HEM-705 was used at ages 53 and 60–64. The auscultatory approach involves measuring systolic and diastolic BP, whereas automated oscillometric devices, such as the Omron HEM-705, extrapolate systolic and diastolic BP from the measured mean arterial pressure. The Hawksley Random Zero sphygmomanometer was designed to reduce observer bias.² However, as first reported by O’Brien³ and confirmed by others,² it underestimates BP, on average by as much as 3.8 mmHg systolic and 7.5 mmHg diastolic.⁴ This underestimation increases with higher BP levels.⁵ Based on a German study,⁶ Ghosh and colleagues applied linear regression analysis including sex, age, and BP level as covariables to adjust the random zero measurements and to achieve compatibility with the later oscillometric readings. Although Ghosh and colleagues might have had no alternative, one wonders to what extent a study done in Germany with different devices is applicable to MRC-NSHD and whether auscultatory and oscillometric estimates of BP can be used interchangeably. The authors might have considered more robust ways for adjusting for the use of two different devices, for instance by setting up their own reproducibility study or by comparing BP slopes obtained before and after age 53.

Another potentially clinically important observation emerging from the study of Ghosh et al.¹ is that people with treated hypertension had higher LVMI even after adjustment for current BP. However, the MRC-NSHD report provided no information on the persistence of treatment over time, the BP levels reached on treatment, or exception made for the treatment status at 60–64 years on the drug classes prescribed. Nevertheless, Ghosh’s observations is in line with the results of the Pressioni Arteriose Monitorate E Loro Associazioni (PAMELA) study.⁶ The 2051 participants were categorized based on their office, home, or 24 h BP into normotensive individuals and patients with hypertension, who were untreated, treated but not controlled, or treated and controlled.⁶ Compared with the normotensive group, LVMI was higher not only in untreated hypertensive patients, but also in treated uncontrolled patients and even in treated and controlled patients (79.7 vs. 91.3, 103.4 and 94.3 g/m², respectively). The same was true for the prevalence of left ventricular hypertrophy (4.2 vs. 14.3, 28.7, and 19.0%, respectively).⁶ Ghosh and colleagues speculated that an elevated BP in midlife causes a ‘legacy’ of cardiac damage including interstitial and perivascular fibrosis that may be difficult to reverse even if BP is subsequently well controlled.
with medication. In line with this hypothesis, we previously demonstrated that normalization of the ambulatory BP on antihypertensive drug treatment does not eliminate the lifetime cardiovascular burden associated with the previous elevated BP, perhaps because blood pressure normalization by itself does not address other risk factors that cluster with hypertension.

Vasan and colleagues evaluated association of current BP (at baseline), recent antecedent BP (average of readings for all available examinations 1–10 years before baseline), and remote antecedent BP (average for all available examinations 11–20 years before baseline) with the 10-year cardiovascular risk in 2313 Framingham participants. They reported that antecedent BP is a major determinant of the future cardiovascular risk above and beyond current BP. In a subsequent report, the Framingham investigators noticed that higher midlife BP and body mass index predict heart failure later in life. A pooled analysis of seven US cohorts involved 61 585 subjects, 700 000 person-years of follow-up starting at age 55, and prior BP data over an average of 14 years. Individuals who maintained or decreased their BP to normal levels had the lowest remaining lifetime risk for cardiovascular disease, 22–41%, compared with individuals who had or developed hypertension by 55 years of age, 42–69%. Among 4217 Framingham study participants, who underwent up to four serial echocardiographic examinations, sex, age, body mass index, systolic BP, antihypertensive treatment, smoking, and diabetes mellitus were the determinants of tracking of left ventricular mass over the adult life course. At variance with Ghosh’s findings, women experienced a steeper increase in left ventricular mass with advancing age and increasing body mass index compared with men. We also found in a large international database that the risk associated with the level of the ambulatory BP increased more steeply in women than in men (Figure 1).

In conclusion, the report by Ghosh and colleagues confirms the results of previously published cohort studies that all showed that BP early in life is a major determinant of adverse cardiovascular outcomes later in life. Investigators in the Global Burden of Diseases Study 2010 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. As demonstrated by Ghosh et al. and other investigators, antihypertensive drug treatment does not completely reverse the risk associated with the BP burden early in life, in particular when the BP load is allowed to persist for many years or in the presence of other risk factors. The take home message of Ghosh’s report is therefore an appeal to overcome therapeutic inertia. Patients and caregivers should commence and maintain antihypertensive drug treatment as soon as the diagnosis of hypertension is confirmed, preferably by ambulatory BP monitoring, and should not rest until BP levels are at goal. In contrast to Ghosh’s contention, women are a particularly vulnerable group and represent a group in whom early treatment of hypertension represents an opportunity to increase years and quality of life.

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**Figure 1** Changes in the incidence of mortality and cardiovascular (CV) events that would be associated with a 1–SD (standard deviation) decrease in the 24 h systolic blood pressure (BP) (A) or in the night-time BP (B) in women (circles) and men (squares). Estimates were adjusted for cohort, age, body mass index, smoking and drinking, serum total cholesterol, a history of CV disease, the presence of diabetes mellitus, and antihypertensive drug treatment at baseline. *P*-values indicate significant sex differences. Reproduced with permission from Boggia et al.
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**References**


