Decisions about antihypertensive treatment should focus on reducing cardiovascular risk

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Epidemiological studies[1,2] provide strong evidence for an association between high blood pressure and fatal cardiovascular complications, and interventional studies have shown that antihypertensive treatments reduce cardiovascular events and all-cause mortality.[3,4] Although the target blood pressure for patients with hypertension receiving treatment in the current US guidelines[5] is less than 130/80 mm Hg and European recommendations indicate achieving 120–129/70–79 mm Hg for people younger than 65 years (and 130–139/70–79 mm Hg for those ≥65 years),[6] other guidelines such as those from the UK[7] recommend higher target values for treatment. Thus, threshold blood pressure levels for initiating therapy and target blood pressure levels with treatment remain controversial. Furthermore, the effect of initial blood pressure on outcome, and the benefit for patients treated in primary versus secondary prevention settings have not been settled.[4,8]

In *The Lancet*, a study by the Blood Pressure Lowering Treatment Trialists' Collaboration (BPLTTC; Oxford University, Oxford, UK)[9] adds important information for these questions. The investigators did a meta-analysis of individual participant-level data from 48 major randomised clinical trials (≥1000 patient-years per allocated group, assessing drug *vs* placebo, drug *vs* drug, or more *vs* less intensive treatment), comprising 344 716 patients within the BPLTTC. The investigators (1) assessed the effect of blood pressure-lowering treatment when blood pressure before treatment is below typical threshold values for detecting or treating hypertension; and (2) compared the effects of antihypertensive treatment in patients with and without concomitant cardiovascular comorbidity. Studies done exclusively in patients with heart failure or in acute settings were excluded.

Participants were divided into those with a previous diagnosis of cardiovascular disease and those without cardiovascular comorbidity at baseline (ie, any reports of stroke, myocardial infarction, or ischaemic heart disease before randomisation), and further divided into groups according to systolic blood pressure at study entry (<120, 120–129, 130–139, 140–149, 150–159, 160–169, and ≥170 mm Hg). An entry blood pressure of 139 mm Hg or lower was noted in 37% of patients with prevalent cardiovascular comorbidity and 18% of patients with no comorbidity. In patients with cardiovascular comorbidity, 75% had a history of ischaemic heart disease, 36% stroke, 12% peripheral artery disease, and 27% diabetes. Mean age was 65 years, with 33% and 49% of the female participants with and without cardiovascular disease, respectively. The studies were done in Asia, Australia, New Zealand, North America, and Europe, suggesting that the study population had a broad representation of different ethnicities. The primary outcome was a major cardiovascular event, defined as a composite of fatal and non-fatal stroke, fatal or non-fatal ischaemic heart disease, or heart failure causing death or requiring admission to hospital. Median follow-up was 4·1 years, and mean blood pressure at study entry was 146/84 mm Hg and 157/89 in patients with and without previous cardiovascular disease, respectively.

The results showed similar treatment effects on cardiovascular events in patients with (secondary prevention) and without (primary prevention) prevalent cardiovascular comorbidity.[9] Thus, overall hazard ratios (adjusted to a 5 mm Hg reduction in systolic blood pressure) for the composite primary outcome of a major cardiovascular event were 0·89 (95% CI 0·86–0·92) and 0·91 (0·89–0·94) in patients with and without cardiovascular comorbidity, respectively. A reduction in systolic blood pressure also reduced the risk of stroke, ischaemic heart disease, heart failure, and cardiovascular death regardless of cardiovascular comorbidity. Furthermore, the benefit of treatment was similar across all strata of entry blood pressure, with no difference between patients with and without cardiovascular comorbidity. Additional analyses of absolute risk reductions confirmed these results.

The study by the BPLTTC[9] represents the largest meta-analysis so far of individual participant-level data for the effects of antihypertensive treatment stratified by initial blood pressure and prevalent cardiovascular disease. The results showed that the benefit of antihypertensive drug treatment is proportional to the intensity of blood pressure reduction, and that the magnitude of relative (and absolute) risk reduction is similar across baseline

systolic blood pressure levels from less than 120 mm Hg to more than 170 mm Hg, extending observations from epidemiological studies.[1] In agreement with previous reports,[3,4] antihypertensive treatment appears to reduce incident stroke and heart failure by a greater extent than ischaemic heart disease. However, the reported benefit at low entry systolic blood pressure in patients with a high proportion (75%) of ischaemic heart disease suggests that the risk of blood pressure lowering in this group of patients (ie, a J-curve for risk) might not be a problem in most patients.

Of note, this systematic review could not include all eligible trials, which is an inherent limitation of all individual participant data meta-analyses. However, the investigators assessed the risk of acquisition bias, and also did sensitivity analyses excluding trials, without important effects on their findings. The findings might not be generalisable to patient groups with concomitant conditions not studied in these analyses (eg, heart failure).

The similar relative benefits of treatment in primary and secondary prevention presented in the study by the BPLTTC[9] indicate that the cardiovascular risk of an individual will be a major determinant of the absolute benefit of treatment, confirming the importance of risk assessment in individual patients.[10] These findings have important implications for clinical practice, and suggest that antihypertensive treatment might be considered for any person for whom the absolute risk for a future cardiovascular event is sufficiently high. This suggestion calls for simple, reliable multivariable risk prediction tools made readily available in the electronic health record systems used by health-care providers. The use of patient self-reported computerised medical history taking could facilitate such development.[11] Taken together, decisions about offering people antihypertensive treatment are all about cardiovascular risk reduction.

I report research grants to the Karolinska Institute from Amgen, Medtronic, and ReCor Medical, all outside the area of work commented on here.

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