PERSPECTIVES IN HYPERTENSION

The ESPRIT trial

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Lowering blood pressure (BP) is one of the most effective treatments to prevent cardiovascular events. Uncertainty exists about whether targeting standard office systolic blood pressure (SBP) <120 mm Hg is better than <140 mm Hg due to limited and conflicting evidence from randomized controlled trials. The Systolic Blood Pressure Intervention Trial (SPRINT) is the only trial that proved targeting SBP <120 mm Hg prevents more major vascular events than <140 mm Hg in patients with high cardiovascular risk but without diabetes or stroke.[1] In contrast, The Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial compared the two SBP targets in patients with diabetes and the Recurrent Stroke Prevention Clinical Outcome (RESPECT) trial in those with history of stroke, and both obtained nonsignificant results.[2,3] The differences in results among these trials might be due to the statistical underpower of ACCORD and RESPECT, the confounding effect of factorial design, the interactions by diabetes status and history of stroke, or different BP measurements. Therefore, given the above uncertain benefit and potential harm, most current clinical guidelines do not recommend lowering SBP to less than 120 mm Hg.[4-7] To provide more evidence on comparing the efficacy and safety of the two SBP targets, we conducted the Effects of Intensive Systolic Blood Pressure Lowering Treatment in Reducing Risk of Vascular Events (ESPRIT) trial.[8]

ESPRIT is an open-label, blinded-outcome, randomized controlled trial conducted at 116 sites (103 hospitals and 13 community medical centres) in China. All data in the trial were processed electronically. We used an online system and a minimized randomization program to randomly allocate participants to either intensive treatment (targeting standard office SBP <120 mm Hg) or standard treatment (targeting standard office SBP <140 mm Hg) in a 1:1 ratio. Then we followed up the participants regularly. At each clinic visit, a trained investigator used an electronic BP monitor to measure the standard office BP. We titrated participants' antihypertensive medications to achieve the set SBP target or the lowest tolerable BP. The COVID-19 pandemic caused a 3-month delay for the intensive treatment group to reach the target SBP, so we extended the follow-up by 3 months.9 The primary outcome was major vascular events, i.e., a composite of myocardial infarction, coronary or non-coronary revascularization, hospitalization/emergency room visit for heart failure, stroke, or death from cardiovascular causes.

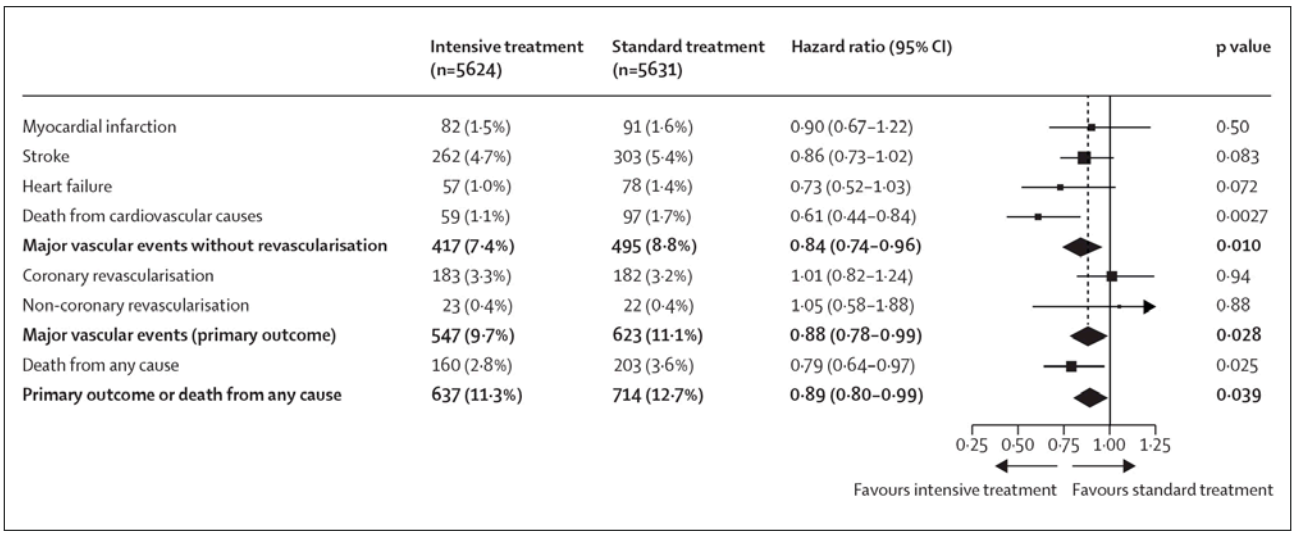
We enrolled 11,255 participants with high cardiovascular risk and with or without diabetes or previous stroke during 2019-2020. Mean age was 64.6 years, 41.3% were women and 58.7% were men, and a history of diabetes was reported by 38.7% of the participants and stroke by 26.9%. The mean baseline SBP in the intensive and standard treatment groups were 146.8±10.5 mm Hg and 147.0±10.7 mm Hg, respectively. Throughout the follow-up (except the first 3 months for titration), we achieved a mean SBP of 119.1±11.1 mm Hg in the intensive treatment group, and 134.8±10.5 mm Hg in the standard treatment group.

During a median of 3.4 years of follow-up, the primary outcome event occurred in 547 (9.7%) participants in the intensive treatment group and 623 (11.1%) in the standard treatment group. The intensive treatment reduced 12% risk of major vascular events. There was no heterogeneity of

effects by diabetes status, duration of diabetes, or history of stroke. To prevent a primary outcome event and a cardiovascular death, 75 and 148 patients need to be treated for 3 years, respectively. The individual components of primary outcome showed differential effects. Death from cardiovascular causes occurred in 59 participants (1.1%) from Intensive Group and in 97 (1.7%) from Standard Group (HR 0.61; 95% CI 0.44-0.84). The between-group differences of myocardial infarction, heart failure, and stroke were similar with the primary outcome but not statistically significant. However, the rates of coronary revascularization and non-coronary revascularization were almost the same between groups. The risks of death from any cause (HR 0.79; 95% CI 0.64-0.97) and composite of primary outcome or death from any cause (HR 0.89; 95% CI 0.80-0.99) were lower in Intensive Group (Figure).

Consistent with SPRINT, we observed that the intensive treatment increased risk of sustained renal function decline.[1] However, few participants developed end-stage renal disease. Serious adverse events of syncope occurred more frequently in the intensive treatment group (0.4%) than in standard treatment group (0.1%). There was no significant between-group difference in the serious adverse events of hypotension, electrolyte abnormality, injurious fall, or acute kidney injury. Moreover, the intensive treatment group experienced much fewer of these serious adverse events in our trial than previous trials. The better safety might be attributed to the nature of the study population or treatment.

Our trial has a number of strengths to facilitate reliable assessments of moderate but important treatment effects, including a large sample size, high adherence to intervention, few participants lost to follow-up, and a large number of clinical outcomes. Our study was conducted at both hospital and community settings in diverse economic–geographic regions. Our trial shows that treatment on a regular follow-up basis, with committed personnel, and common,



Primary outcome and secondary outcomes

The primary outcome is a composite cardiovascular outcome of myocardial infarction, coronary or non-coronary revascularisation, hospitalisation or emergency room visit for new-onset heart failure or acute decompensated heart failure, stroke, or death from cardiovascular causes. Heart failure is defined as hospitalisation or emergency room visit for new-onset heart failure or acute decompensated heart failure. The prespecified secondary outcomes included components of the primary composite outcome, death from any cause, a composite of the primary outcome or death from any cause. The analysis for the outcome of major vascular events without revascularisation was a post-hoc analysis. A single patient can have multiple events and therefore can contribute information to more than one row. The size of each square for hazard ratio is proportional to the precision of the estimates (with larger boxes indicating a greater degree of precision), the horizontal lines represent 95% CIs, and the dashed vertical line indicates the overall hazard ratio for the effect of intensive treatment on the first major vascular event. For composite outcomes, hazard ratios and their corresponding 95% CIs are represented by bold text and diamonds.

accessible, and affordable drugs is feasible to benefit hypertensive patients with high risk of cardiovascular disease.

In conclusion, targeting SBP of less than 120 mm Hg, as compared with that of less than 140 mm Hg, prevents major vascular events and death with minor excess risk in patients with hypertension at high cardiovascular risk, regardless of the status of diabetes or history of stroke.

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