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Is the Evidence Provided by the SPRINT Trial Solid Enough to Support a Systolic Blood Pressure Threshold of 120 mmHg?



¿La evidencia aportada por el estudio SPRINT es suficientemente sólida para sostener un umbral de presión arterial sistólica de 120 mmHg?

To the Editor,

We have read with great interest the article by Barrios and Escobar,¹ which offers a critique of the results of the SPRINT² trial, mainly based on the method used to take blood pressure (BP). We also believe it pertinent to highlight other features of the study.

The weakest point of the SPRINT trial is probably its early termination due to benefit, which is a potential cause of overestimating the magnitude of the effect and increasing the probability that the observed differences are due to chance or random error. This randomized clinical trial (RCT) was planned for a follow-up of 5 years, but was stopped after 3.26 years due to benefit.³ Some RCTs with an unexpectedly large beneficial effect were initially continued according to the protocol and the final results showed no differences between groups.⁴ When other contemporary RCTs with intensive BP control were incorporated into a meta-analysis, Yusuf et al.⁵ found that this strategy reduced the primary outcome by 15%, which was less than the 25% reduction reported in the SPRINT trial.² If this trial had not been stopped, it is likely that the relative benefit would have been lower and the difference in the primary outcome may not have been significant. In fact, an analysis of the components of the primary outcome shows that the benefit of the SPRINT trial was achieved due to a reduction of acute heart failure (AHF) and cardiovascular (CV) mortality, without a reduction of stroke or coronary syndrome. There are 2 reasons for the differences in AHF: *a*) the use of diuretics in the intensive BP control group was significantly higher (67% vs 42.9%); and *b*) to maintain the BP target in the standard BP control group, 87% of the participants decreased or discontinued a drug they previously received, despite being asymptomatic. The clinical impact of this action is uncertain and potentially harmful.

Although the reduction of CV mortality was significant, the absolute number of events was low: 37 in the intensive group and 65 in the standard group. The application of a Fragility Index⁶ shows that the addition of 8 events to mortality in the intensive group makes the difference nonsignificant, suggestive of a weakness of the study. The number of patients needed to be treated to prevent 1 CV death in the high-risk population would be 167 patients (95% confidence interval, 116–500) over 3.26 years. There are 3 possible reasons why the reduction in the number of CV deaths was due to the random error: *a*) as mentioned, the trial was stopped early; *b*) the loss of participants was high: 5% dropped out and more than half of them (2.62%, *n* = 245) were completely lost to follow-up; and *c*) as causes of death, 71 were grouped as “unclassifiable” or “not yet classified” deaths.

A major concern when pursuing intensive BP control targets is the safety of the intervention itself. In the SPRINT trial there was a significant increase in arterial and orthostatic hypotension, syncope, electrolyte abnormalities, and acute renal failure. If all the severe adverse effects that required visits to emergency services or hospitalization in the intensive group are counted, then the number of patients needed to treat to harm was 19. That is, for every 19 patients treated to achieve a systolic BP < 120 mmHg, it was predicted that 1 patient should attend emergency services or be hospitalized due to severe adverse drug reactions.

Finally, the external validity of an RCT represents the possibility of generalizing the results independently of their internal validity. The SPRINT trial excluded patients with diabetic mellitus, stroke or cardiovascular events, left ventricular ejection fraction < 35%, symptoms of AHF in the last 6 months, and patients “not adherent to pharmacological treatment”. Deep reflection on potential benefits and risks is needed before generalizing the results.

In conclusion, BP is a continuous variable that is categorized for pragmatic purposes; therefore, aiming for a target of < 140/90 mmHg is beneficial for some subgroups of patients. The challenge of evidence-based medicine is to integrate population-based knowledge with the distinctive characteristics of each patient in order to define an “individualized” strategy that also incorporates the expectations and preferences of each person.

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