Il nuovo studio 'SPRINT' consiglia di abbassare i valori pressori sistolici a sotto i 120 mm Hg in nei pz con HTN (senza diabete)

Sommario e commenti

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AHA scientific session Orlando (***UPDATED WITH COMMENTARY***) — Lower rates of cardiovascular events and all-cause mortality are associated with targeting systolic blood pressure of less than 120 mm Hg vs the standard, and guideline-recommended, rate of less than 140 mm Hg in patients at increased CV risk, according to full findings from the highly anticipated Systolic Blood Pressure Intervention Trial (SPRINT)[1]. Has been presented here at the AHA 2015 and in simultaneous publication in the *New England Journal of Medicine.*

SPRINT, which was funded by the National Institutes of Health (NIH) and included more than 9000 US patients who were hypertensive but not diabetic, showed that the lower target group of less than 120 mm Hg systolic blood pressure had a 25% lower relative risk of the primary composite end point of MI, ACS, stroke, acute decompensated HF, and CV death vs the group with a target of less than 140 mm Hg.

In addition, the lower-target group had 27% lower risk of all-cause mortality and 43% lower risk of CV death. However, this group also had higher adverse events such as hypotension, syncope, and acute kidney injury (AKI) or failure.

In an accompanying editorial[2], Drs Vlado Perkovic and Anthony Rodgers (University of Sydney, Australia) note that trials aren't usually all good or all bad and that the serious adverse-event rates here "appear unlikely" to outweigh the overall benefits. "Current guidelines and guideline processes [will] require revision," they write.

The SPRINT participants were enrolled between November 2010 and March 2013 at 102 clinical sites. All had a systolic blood pressure of 130 to 180 mm Hg, were deemed at risk of CV events, and were at least 50 years of age; 28% were older than 75 years, and 35% were women. Choice of antihypertensive medications to achieve blood-pressure control was left to physicians and patients in this open-label, target-based study.

Roughly half of the participants were randomized to a target systolic blood-pressure rate of less than 120 mm Hg (intensive therapy) and treated with roughly three antihypertensives. The other half had a target blood-pressure rate of less than 140 mm Hg (standard therapy) and received an average of two antihypertensives.

All of the patients underwent clinical and laboratory tests at baseline and at each subsequent 3-month follow-up. Self-reported CVD outcomes were also collected during structured interviews during the follow-ups.

As noted, SPRINT **was stopped early in August 2015 because of its significant reductions in the primary composite end point** and because secondary end points "exceeded the monitoring boundary at two consecutive time points," report the investigators. It was scheduled to end in 2016 after 5 years. Instead, there was a median follow-up of only 3.26 years.

The early stoppage "was a shock to us," said Wright. "We had no idea, because we never saw the open data that the monitoring board saw. When it was stopped early by the [National Heart, Lung, and Blood Institute] NHLBI director, we had to deal with a large number of issues very quickly, including informing the patients and their providers," he said.

"With such a large number of patients, we couldn't keep that secret. So we decided to announce publicly limited results and why the trial was stopped early, to make sure we could control the information that was coming out." He noted that that announcement occurred on September 11, with full presentation of the results occurring less than 8 weeks later.

Practice Changing?

At one year, the intensive group had a mean systolic blood pressure of 121.4 mm Hg vs 136.2 mm Hg in the standard-therapy group. Throughout follow-up, the mean rates were 121.5 mm Hg vs 134.6 mm Hg, respectively.

At the study's end, the intensive-therapy group had a significantly lower composite event rate (1.65% per year) vs the standard therapy group (2.19% per year; hazard ratio [HR] 0.75, 95% CI 0.64–0.89; $P<0.001$), as well as lower all-cause mortality (155 vs 210 deaths; HR 0.73, 95% CI 0.60–0.90; $P=0.003$) and CV-related deaths (37 vs 65; HR 0.57, 95% CI 0.38–0.85; $P=0.005$).

There were no significant between-group differences in "any serious adverse event" (38.3% vs 37.1% for the intensive-therapy group vs the standard-therapy group, respectively).

However, 2.4% of the intensive-therapy group members had hypotension vs 1.4% of the standard-therapy group ($P=0.001$), 2.3% vs 1.7% had syncope ($P=0.05$), 3.1% vs 2.3% had electrolyte abnormalities ($P=0.02$), and 4.1% vs 2.5% had AKI or kidney failure ($P<0.001$). Also, a composite of all treatment-related adverse events was found in 4.7% vs 2.5% of the participants ($P<0.001$).

Wright noted that there were no differences between target groups for injurious falls or bradycardia. In addition, orthostatic hypotension occurred significantly less in the low-target group (16.6% vs 18.3%, respectively, $P=0.01$).

As for the other adverse events noted, "we're talking about just a 1% to 2% increase for those with the lower blood-pressure target," he said. "Also, the patients we were most concerned with, those over the age of 75, tolerated the lower target at least as well as those who were younger."

When asked if the overall results are practice changing, Wright begged off, saying his job was just to report the data. "I feel very comfortable, once all the details of the data are out there, that the providers, the provider community, and the guideline panels can weigh the results from SPRINT, along with other evidence that's out there, to come to a decision on the best way to manage hypertension."

Comments

Perkovic and Rodgers write in their editorial that "the eagerly awaited results" will have far-reaching implications and that a systolic goal of less than 120 mm Hg "is appropriate" for high-CV-risk patients. However, they note that a lot of effort is required to hit this target, including initial combination therapy and frequent office visits.

"SPRINT . . . challenges us to improve blood-pressure management. Success will require a marathon effort," they write.

On the other hand, **Dr Murray Esler** (Baker IDI Heart and Diabetes Institute, Melbourne, Australia) writes in another editorial[3], published today in *Hypertension*, that although "SPRINT promises to transform the clinical practice of antihypertensive drug prescribing," he has his concerns with the study exclusions, noting that excluding diabetics is "a black hole" in the study and limits its applicability.

"Do we now have a new, lower therapeutic target in hypertension clinical care, or is the target 'SPRINT-specific?' " he writes, asking if 120 mm Hg should be the target for patients with systolic blood pressure of 170 or even 200 mm Hg.

"My 45 years of clinical experience in the treatment of patients with more severe grades of hypertension lead me to doubt this," concludes Esler.

"The main issue to me is: does this provide us a universal target that can be used in all patients? The entry blood pressure was modestly elevated," he said. To what extent did that have an effect on the goal? "I would say it did have an impact, and I think the panel agreed with me."

When asked if the live presentation answered some of the concerns mentioned in his editorial, Esler said that the diabetes exclusion "is still a black hole," especially because so many hypertensive patients have comorbid diabetes. "And there's no answer on what to do with them." Still, he said he thinks the trial will and should have an impact on guidelines.

Dr Marc Pfeffer (Harvard Medical School, Boston, MA) was another discussant at the clinical-trials session as well as at an earlier press briefing. He told attendees that SPRINT "is an amazing trial and a triumph." However, physicians "shouldn't expect a 'thank you' from patients when you add another pill to reduce their blood pressure."

Dr Sripal Bangalore (New York University School of Medicine, NY) told that the trial results provided "a very clear message" about the reduction in death, CV death, and heart failure.

However, he noted that when trials are prematurely terminated with large effect sizes, the results might not translate if the trial were to continue and might not translate into real life.

Bangalore, who was not involved with this study, said that even if the reductions aren't as high as 25% in clinical practice, the results do suggest significant benefit. But he was surprised that there was no significant reduction in stroke. "If there was one outcome I would have bet on, it would have been that," he said.

"Also interesting was that half the patients could not achieve the less-than-120 target. If that happened in a large randomized trial, I would imagine that would be really difficult to achieve in real-world practice," he said, adding that although the adverse events were somewhat worrisome, the absolute rates were pretty low.

In another paper, which was published today in the *Journal of the American College of Cardiology*, **Dr Adam P Bress** (University of Utah, Salt Lake City) and colleagues report their findings on how generalizable the SPRINT trial is, based on data from the 2007–2012 National Health and Nutrition Examination Survey[4].

They found that 16.8 million US adults (7.6%) met the trial's eligibility criteria, as did 8.2 million (16.7%) of those with treated hypertension. For both groups, the eligibility criteria was higher for patients who were older, male, and non-Hispanic white. The editorialists note that the findings show that a large group of US adults could be potentially affected by SPRINT's results.

"I think it all comes down to risks/benefits. And I think we need to partner with patients," said Bangalore. "For some, it's hard to get them to take one medication, while others are really compliant and wouldn't mind taking three medications if it meant reaching the reduced outcomes. At the end of the day, it's about individualizing the issues."

SPRINT was funded by the National Institutes of Health.

References

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