To the Editor:

We read the recent article by Peralta et al.\(^1\) that was published in Circulation with great interest. In their post hoc analysis of the SPS3 study (Secondary Prevention of Small Subcortical Strokes), they found that, in patients with a prior lacunar stroke, treating to lower systolic blood pressure (SBP) targets (SBP<120 mmHg) led to a higher likelihood of rapid kidney function decline, although this decline was not associated with worse cardiovascular outcomes. They also found that, although treating to a higher SBP target (SBP<140 mmHg) led to less rapid kidney function decline, the rapid decliners in this group were associated with a higher risk of poor cardiovascular outcomes. These findings were contrary to the expectation that rapid decliners in both groups would experience a higher risk of poor cardiovascular outcomes in comparison with nondecliners.

The authors provide some explanations for the results in their discussions, including the possibility that intense SBP lowering may ultimately be cardioprotective in decliners. We proffer another explanation: proteinuria. A recent post hoc analysis of the CRIC study (Chronic Renal Insufficiency Cohort) showed that proteinuria predicts cardiovascular outcomes more powerfully than glomerular filtration rate.\(^2\) The SPS3 study did not report the level of proteinuria in any of the groups studied, and this might have been the independent variable propelling the higher risk of poor cardiovascular outcomes in the rapid decliners of the higher SBP target group. It is very likely that data on proteinuria in both groups, even if measured semiquantitatively, would be invaluable in interpreting these findings.

It is also possible that the findings on cardiovascular outcomes obtained were attributable to a differential use of antihypertensive drugs that reduce proteinuria between the higher-target SBP decliners and the lower-target SBP decliners. Reducing proteinuria in chronic kidney disease with drugs such as angiotensin-converting enzyme inhibitors and angiotensin receptor blockers has been shown to improve cardiovascular outcomes.\(^3\) It will be interesting to see whether the authors have any data on the differential use of these medications between both groups. If such a difference explains these paradoxical results, then it will reinforce the philosophy that how hypertension is treated in the setting of declining glomerular filtration rate is more important than the absolute numbers targeted.

**DISCLOSURES**

None.

**AFFILIATION**

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REFERENCES


Letter by Mezue et al Regarding Article, "Effect of Intensive Versus Usual Blood Pressure Control on Kidney Function Among Individuals With Prior Lacunar Stroke: A Post Hoc Analysis of the Secondary Prevention of Small Subcortical Strokes (SPS3) Randomized Trial"

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