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Renal function and intensive blood pressure lowering in high-risk adults without diabetes: insights from the Systolic Blood Pressure Intervention Trial (SPRINT)

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Background: The Systolic Blood Pressure Intervention Trial (SPRINT) found that intensive blood pressure (BP) lowering reduced the rates of cardiovascular events and mortality but increased the risk of certain adverse events, in patients with and without chronic kidney disease at baseline. However, it is unclear whether intensive BP management is well-tolerated and modifies risk uniformly across the entire spectrum of renal function.
Purpose: To assess the relationship between renal function, treatment response to intensive BP lowering, and cardiovascular (CV) outcomes.
Methods: SPRINT was a randomized, controlled trial in which 9,361 individuals ≥50 years of age, at high CV risk but without diabetes who had a systolic BP (SBP) 130–180 mmHg, were randomized to intensive (target SBP <120mmHg) or standard antihypertensive treatment (target SBP <140mmHg). The primary efficacy endpoint was the composite of acute coronary syndromes, stroke, acute decompensated heart failure, or death from CV causes. The primary safety endpoint was the composite of serious adverse events (SAE). Renal function was assessed using the estimated glomerular filtration rate (GFR), calculated with the Modification of Diet in Renal Disease equation. We first assessed whether a linear association was present between eGFR and clinical endpoints using restricted cubic splines. We then examined the prognostic implications of eGFR, unadjusted and adjusted for demographic, clinical, and laboratory variables. We further explored the effects of intensive BP lowering across the eGFR spectrum.
Results: Baseline eGFR was available for 9,324 (>99%) individuals. Mean eGFR was similar between the two groups (intensive group 71.8 ml/min/1.73m^2 vs. standard group 71.7 ml/min/1.73m^2; P=0.92). Median follow-up was 3.3 years (range 0–4.8), with 561 primary efficacy events (6%) and 3,522 SAE (38%) recorded during the study period. Baseline eGFR was non-linearly associated with the risk of the primary efficacy endpoint, death from CV causes, death from any cause, acute decompensated heart failure, SAE, electrolyte abnormality, and acute kidney injury (test for non-linearity, P<0.05; test for overall trend, P<0.001) and remained significantly associated with all tested endpoints upon multivariable adjustment (P<0.05). Baseline eGFR significantly modified the effects of intensive BP lowering on the primary efficacy endpoint (P=0.02), acute decompensated heart failure (P=0.01), SAE (P=0.01), and acute kidney injury (P=0.04). The Figure shows treatment effects (hazard ratios) across the spectrum of eGFR for these four endpoints. P-values are for the interaction between eGFR and treatment effect. Significant interactions were not detected for other endpoints.
Conclusions: In SPRINT, lower eGFR was associated with a greater risk of both CV events and SAE. Patients with higher eGFR appeared to derive more benefit from intensive BP lowering while the relationship with safety events was complex.

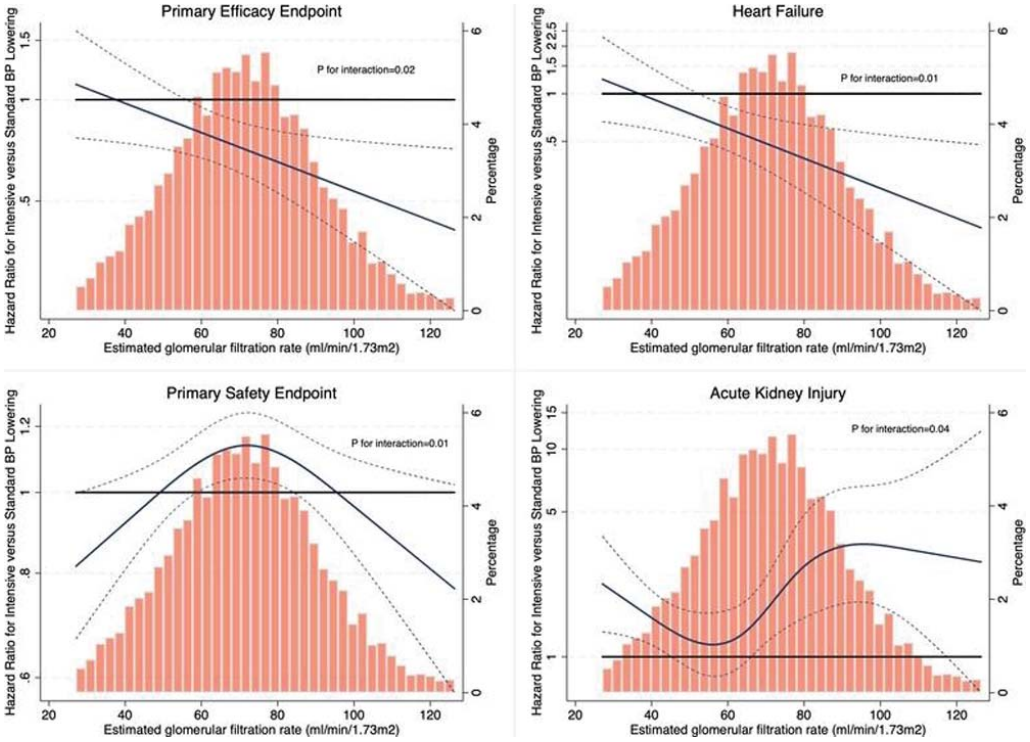

Figure 1