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Changes in Natriuretic Peptide Levels and Subsequent Kidney Function Decline in SPRINT

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Abstract

Rationale & Objective: Novel approaches to the assessment of kidney disease risk during hypertension treatment are needed because of the uncertainty of how intensive blood pressure (BP) lowering impacts kidney outcomes. We determined whether longitudinal N-terminal pro–B-type natriuretic peptide (NT–proBNP) measurements during hypertension treatment are associated with kidney function decline.

Study Design: Prospective observational study.

Setting & Participants: 8,005 SPRINT (Systolic Blood Pressure Intervention Trial) participants with NT–proBNP measurements at baseline and 1 year.

Exposure: 1-year change in NT–proBNP categorized as a ≥25% decrease, ≥25% increase, or <25% change (stable).

Outcome: Annualized change in estimated glomerular filtration rate (eGFR) and ≥30% decrease in eGFR.

Analytical Approach: Linear mixed-effect and logistic regression models were used to evaluate the association of changes in NT–proBNP with subsequent annualized change in eGFR and ≥30% decrease in eGFR, respectively. Analyses were stratified by baseline chronic kidney disease (CKD) status.

Results: Compared with stable 1-year NT–proBNP levels, a ≥25% decrease in NT–proBNP was associated with a slower decrease in eGFR in participants with CKD (adjusted difference, 1.09%/y; 95% Cl, 0.35–1.83) and without CKD (adjusted difference, 51 %/y; 95% Cl, 0.21–0.81; $P = 0.4$ for interaction). Meanwhile, a ≥25% increase in NT–proBNP in participants with CKD was associated with a faster decrease in eGFR (adjusted difference, −1.04%/y; 95% Cl, −1.72 to −0.36) and risk of a ≥30% decrease in eGFR (adjusted odds ratio, 1.44; 95% Cl, 1.06–1.96); associations were stronger in participants with CKD than in participants without CKD ($P = 0.01$ and $P < 0.001$ for interaction, respectively). Relationships were similar irrespective of the randomized BP arm in SPRINT ($P > 0.2$ for interactions).

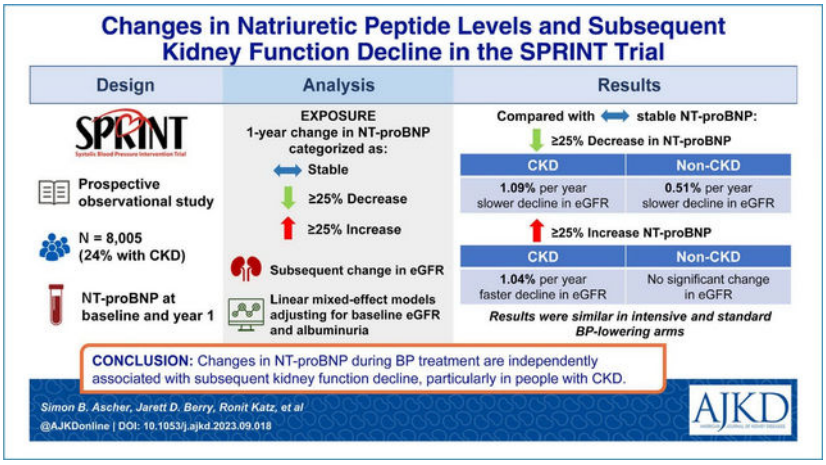
Limitations: Persons with diabetes and proteinuria >1 g/d were excluded.

Conclusions: Changes in NT–proBNP during BP treatment are independently associated with subsequent kidney function decline, particularly in people with CKD. Future studies should assess whether routine NT–proBNP measurements may be useful in monitoring kidney risk during hypertension treatment.

PLAIN-LANGUAGE SUMMARY

N-terminal pro–B-type natriuretic peptide (NT–proBNP) is a biomarker in the blood that reflects mechanical stress on the heart. Measuring NT–proBNP may be helpful in assessing the risk of long-term losses of kidney function. In this study, we investigated the association of changes in NT–proBNP with subsequent kidney function among individuals with and without chronic kidney disease. We found that increases in NT–proBNP are associated with a faster rate of decline of kidney function, independent of baseline kidney measures. The associations were more pronounced in individuals with chronic kidney disease. Our results advance the notion of considering NT–proBNP as a dynamic tool for assessing kidney disease risk.

Graphical Abstract



In nondiabetic individuals with hypertension and at high risk of cardiovascular disease (CVD), the Systolic Blood Pressure Intervention Trial (SPRINT) demonstrated that targeting a systolic blood pressure (SBP) of <120 mm Hg compared with <140 mm Hg led to significant reductions in CVD events and all-cause death.[1] However, the effect of lower SBP targets on kidney outcomes was less clear. Although randomization to intensive SBP

lowering in SPRINT led to greater dereases in estimated glomerular filtration rate (eGFR) in the first months of the trial, these acute changes are most likely related to hemodynamic changes rather than intrinsic kidney injury. However, even after these acute changes, participants in the intensive SBP lowering arm experienced a greater risk of incident chronic kidney disease (CKD) and a slightly faster decrease in eGFR compared with the standard am.[2–6] Given the CVD and mortality benefits of intensive SBP lowering and the central role hypertension is believed to play in the development and progression of CKD, novel approaches are needed to understand kidney disease risk during hypertension treatment.

Subclinical elevations in N-terminal pro–B-type natriuretic peptide (NT–proBNP), a measure of cardiac wall stress and neurohormonal activation, are common in the general population and have strong associations with CVD and early death.[7–9] Previous studies have shown that single NT–proBNP measurements are associated with increased risk of incident CKD and CKD progression.[10–25] However, it is unknown whether changes in NT–proBNP levels during hypertension treatment can aid in the assessment of kidney disease risk.

In this ancillary study of SPRINT, we evaluated associations of baseline and 1-year changes in NT–proBNP with subsequent kidney function decline. We also evaluated whether these associations varied by baseline CKD status and randomization to intensive versus standard SBP lowering. We hypothesized that higher baseline levels and greater 1-year increases in NT–proBNP would be associated with faster decreases in eGFR independent of clinical characteristics, randomized treatment arm, and baseline eGFR and albuminuria.

Methods

Study Design

The design and protocol of SPRINT have been reported previously.[1,26] In brief, SPRINT was an National Institutes of Health–funded, open-label clinical trial that randomized participants with hypertension to an intensive SBP target of <120 mm Hg versus a standard SBP target of <140 mm Hg, with individual patient management at the discretion of the trial investigators. Inclusion criteria were age at least 50 years, SBP 130–180 mm Hg, and high CVD risk (defined as prior clinical or subclinical CVD other than stroke, CKD [eGFR 20–59 mL/min/1.73 m^2], age ≥75 years, or 10-year CVD risk >15% based on Framingham risk score). Key exclusion criteria included diabetes mellitus, prior stroke or transient ischemic attack, eGFR <20 mL/min/1.73 m^2, symptomatic heart failure, or left ventricular ejection fraction <35%. A total of 9,361 participants were enrolled between November 2010 and March 2013 across 102 sites in the United States and Puerto Rico. The SPRINT protocol included a baseline visit and follow-up visits monthly for the first 3 months and then every 3 months thereafter. The trial was stopped early on the recommendation of the data and safety monitoring board, which noted substantive evidence of treatment benefits for CVD events and mortality during their regularly scheduled interim evaluation of the data.

Baseline and 12-month concentrations of NT–proBNP were measured in 8,027 SPRINT participants. We excluded 22 participants without at least one follow-up eGFR measurement after the baseline measurement. SPRINT was approved by the institutional review boards at each participating study site, and all participants provided written informed consent.

This ancillary study was approved by the institutional review boards at the University of Texas Southwestern Medical Center; the University of California, San Francisco; the San Francisco Veterans Affairs Health Care System; and the Veterans Affairs San Diego Healthcare System.

Exposure of Interest

Blood specimens were collected at the baseline and 12-month study visits in serum separator tubes, processed immediately, and stored at −80°C until NT–proBNP measurement was performed at the SPRINT Central Laboratory (University of Minnesota, Minneapolis, MN). NT–proBNP was measured from freshly thawed serum samples using an electrochemiluminescence immunoassay on the Cobas 6000 platform (Roche Diagnostics) as previously described.[27] The NT–proBNP assay has interassay coefficients of variation of 2.9% at 140.3 pg/mL and 2.7% at 4,563 pg/mL, with a lower limit of detection of 5 pg/mL. Three percent of NT–proBNP levels were below the lower limit of detection; we assigned these measurements a value of 3.5 pg/mL, equivalent to the lower limit of detection divided by the square root of 2. Consistent with our previous work, baseline NT–proBNP was modeled as a continuous log-linear predictor and according to sex-specific tertiles, and the 1-year change in NT–proBNP was categorized as a ≥25% decrease, ≥25% increase, or <25% change (ie, stable) relative to the baseline NT–proBNP level on the original scale (ie, not log-transformed).[27,28] For analyses using 1-year change in NT–proBNP as the exposure, the 12-month study visit was used as the starting point for annualized eGFR slope and ≥30% decrease in eGFR (Fig SI).

Outcomes

The primary outcome of interest was annualized percentage change in eGFR, which was estimated from a linear mixed-effect model based on serial serum creatinine measurements collected at each monthly visit for the first 3 months and then every 3 months thereafter. Participants were followed until death or the last available study visit before the trial was stopped in August 2015. The secondary outcome was a ≥30% decrease in eGFR. Serum creatinine was measured at the SPRINT Central Laboratory using an enzymatic creatinine method traceable to isotope dilute mass spectrometry (Roche). Estimated GFR was calculated by the 2021 CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation for creatinine.[29]

Covariates

Age, sex, race, ethnicity, medical history, medications, and smoking status (current, former, or never) were obtained by questionnaire. Trained study coordinators measured blood pressure (BP) with an automated oscillometric device (Model 907; Omron Healthcare) according to a standardized protocol and recorded BP as the mean of 3 seated BP measurements taken 1 minute apart after a 5-minute rest period.[30] Body mass index was calculated as weight in kilograms divided by height in meters squared. Fasting serum total cholesterol, high-density lipoprotein cholesterol, triglycerides, and urine albumin and creatinine were measured at the SPRINT Central Laboratory.

Statistical Analyses

Descriptive statistics for baseline characteristics are reported as mean (standard deviation), median (interquartile range), or number (percentage) by sex-specific tertiles of baseline NT–proBNP. NT–proBNP was $\log_2$-transformed to correct its right-skewed distribution.

Linear mixed-effect models with random intercepts, random slopes, and an exchangeable covariance structure were used to evaluate the associations of baseline NT–proBNP and 1-year changes in NT–proBNP levels with annualized eGFR slope. Fixed effects in the models include NT–proBNP, time, and the interactions between NT–proBNP and time, whereby the parameters of time and the interactions represent the annualized eGFR slope. An exchangeable correlation structure assumes that the correlation between any two observations within the same individual is the same regardless of the specific time points or conditions at which the measurements were taken. This assumption simplifies the correlation structure by assuming a constant correlation within individuals, and it is commonly used when there is no prior knowledge or specific information about the correlation patterns within individuals. The linear mixed-effect models used all available eGFR measures for each subject (median number of eGFR measures, 10 [IQR, 9–11]). To allow interpretation of annualized eGFR slope as a percentage, eGFR was log-transformed. Logistic regression models were used to evaluate associations of baseline NT–proBNP and 1-year changes in NT–proBNP levels with a ≥30% decrease in eGFR. SPRINT participants were followed until death or the last available follow-up before the trial was stopped in August 2015.

Models constructed for each outcome were adjusted for the following baseline potential confounders: demographic characteristics (age, sex, race, and ethnicity), randomization arm, kidney disease risk factors (body mass index, smoking status, prevalent CVD, baseline SBP, baseline diastolic BP [DBP], number of antihypertensive medications, diuretic use, and angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker use), baseline eGFR, and baseline urine albumin-creatinine ratio. Analyses of 1-year change in NT–proBNP as the exposure adjusted for the baseline NT–proBNP level. In addition, we adjusted for the first-year change in eGFR and the first-year change in SBP to determine whether the associations of change in NT–proBNP with subsequent change in eGFR were independent of concurrent changes in eGFR and SBP. We also evaluated for interactions by baseline CKD status (eGFR <60 mL/min/1.73 m^2), albuminuria (urine albumin-creatinine ratio ≥30 mg/g), age, sex, prevalent CVD, baseline NT–proBNP level, and randomization arm in multivariable adjusted models using likelihood ratio tests. P values for interactions were adjusted for multiple testing by using the Benjamini-Hochberg procedure and setting the false discovery rate to 5%.[31]

All analyses were conducted using Stata Statistical Software (release 13; StataCorp LP) and SPSS Statistics for Windows (version 26.0; IBM Corp).

Results

Among the 8,005 SPRINT participants included in this analysis, mean age was 68 ± 9 years, 36% were women, and mean baseline eGFR was 74 ±19 mL/min/1.73 m^2. The median NT–proBNP levels were 86 pg/mL at baseline and 82 pg/mL at year 1. Relative to

baseline NT–proBNP levels, year-1 NT–proBNP levels remained stable in 2,362 participants (30%), increased by ≥25% in 2,804 (35%), and decreased by ≥25% in 2,839 (35%). SPRINT participants with higher NT–proBNP levels at baseline were older, more likely to be White, and had higher SBP and lower DBP, more prevalent CVD, lower eGFR, and greater albuminuria (Table SI). Compared with participants with stable 1-year NT–proBNP levels, those with increases in NT–proBNP had similar baseline characteristics, and those with decreases in NT–proBNP were younger, less likely to report White race, and had higher SBP, DBP, and eGFR (Table 1). Baseline CKD was present in 1,958 (24%) participants. Significant interactions by CKD status were identified for associations between baseline NT–proBNP and change in eGFR (P = 0.003 for interaction) and between increases in NT–proBNP and subsequent change in eGFR (P = 0.01 for interaction). Thus, all further analyses are reported stratified by CKD status.

Among 1,958 participants with baseline CKD and 6,047 without CKD, mean baseline eGFRs were 47 ± 10 and 82 ± 13 mL/min/1.73 m^2, respectively, and annualized changes in eGFR during a median of 3.3 years of follow-up were −1.37%/y (95% Cl, −1.54 to −1.20) and −1.24%/y (95% Cl, −1.31 to −1.17), respectively. Median NT–proBNP levels at baseline among participants with and without CKD were 170 pg/mL and 65 pg/mL, respectively. A ≥25% increase or ≥25% decrease in NT–proBNP corresponded to larger absolute NT–proBNP changes in the CKD subgroup (Table S2).

In the CKD and non-CKD groups, the rate of decrease in eGFR was incrementally faster from the lowest to the highest tertile of baseline NT–proBNP (Fig 1). After multivariable adjustment, higher baseline NT–proBNP levels were independently associated with a faster decrease in eGFR, with a stronger association among participants with CKD at baseline (adjusted difference in annualized eGFR slope per 2-fold higher baseline NT–proBNP level: −0.44%/y; 95% Cl, −0.56 to −0.33) than in those without CKD (adjusted difference: −0.10%/y; 95% Cl, −0.14 to −0.05; P = 0.003 for interaction). A similar pattern of results was observed using tertiles of baseline NT–proBNP (Table 2).

We next modeled associations between 1-year NT–proBNP changes and subsequent change in eGFR. Participants with CKD with stable, ≥25% increased, and ≥25% decreased NT–proBNP all had small changes in eGFR from baseline to year 1 (Table S3). However, after year 1, annualized eGFR slope was slowest in the group with a ≥25% decrease in NT–proBNP and fastest among those with a ≥25% increase (Fig 2). Compared with stable NT–proBNP levels, a ≥25% decrease in NT–proBNP was associated with a significantly slower decrease in eGFR in the CKD and non-CKD groups after year 1 (Table 3). Meanwhile, a ≥25% increase in NT–proBNP was associated with a significantly faster decrease in eGFR in the CKD group, but this was not evident in the non-CKD group (P = 0.01 for interaction).

There were 1,552 (19.4%) participants who experienced a ≥30% decrease in eGFR. Among those who did not experience a ≥30% decrease in eGFR, only 155 (2%) died during follow-up. Higher baseline NT–proBNP levels were independently associated with a greater risk of a ≥30% decrease in eGFR, with stronger associations observed in those with baseline CKD (Table S4). A ≥25% decrease in NT–proBNP appeared to be associated with lower risk of a ≥30% decrease in eGFR after year 1 in the non-CKD group (odds ratio, 0.85; 95% Cl,

0.72–1.01), but not in the CKD group (odds ratio, 0.95; 95% Cl, 0.67–1.33). Conversely, a ≥25% increase in NT–proBNP was associated with greater risk of a ≥30% decrease in eGFR in the CKD group (odds ratio, 1.44; 95% Cl, 1.06–1.96), but not in the non-CKD group (odds ratio, 1.02; 95% Cl, 0.87–1.20; P < 0.001 for interaction).

Consistent with the observed interactions by CKD status, higher baseline NT–proBNP levels were more strongly associated with a faster decrease in eGFR among participants with a urine albumin-creatinine ratio ≥30 mg/g versus <30 mg/g (P = 0.003 for interaction; Table S5). The association of 1-year decreases in NT–proBNP (vs stable NT–proBNP) with subsequent decreases in eGFR also appeared stronger among participants with a urine albumin-creatinine ratio ≥30 mg/g, although die interaction was not statistically significant (P = 0.1 for interaction; Table S5). Across the intensive and standard SBP lowering groups, annualized eGFR slope after year 1 was similarly slowest in those with a ≥25% decrease in NT–proBNP (Fig S2). None of the NT–proBNP associations with annualized eGFR slope and risk of a ≥30% decrease in eGFR were modified by randomized treatment assignment (P ≥ 0.1 for all interactions). Participants with a baseline NT–proBNP level ≥125 pg/mL had faster annualized decreases in eGFR after year 1 across all 1 - year NT–proBNP change categories compared with those with a baseline NT–proBNP level <125 pg/mL (Fig S3). However, the associations of a ≥25% increase or a ≥25% decrease in NT–proBNP with a subsequent decrease in eGFR were similar irrespective of baseline NT–proBNP level (P ≥ 0.1 for all interactions). NT–proBNP associations with eGFR decrease also did not vary by age, sex, or prevalent CVD (P ≥ 0.1 for all interactions).

Discussion

In this analysis of SPRINT that included repeated NT–proBNP measurements in more than 8,000 participants, higher baseline NT–proBNP levels and greater 1-year increases in NT–proBNP levels were associated with subsequent decreases in eGFR independent of clinical characteristics, randomized treatment assignment, and baseline eGFR and albuminuria. These associations were stronger among participants with CKD than in those without CKD.

Previous studies have shown that higher single NT–proBNP measurements are associated with more rapid kidney function decline and with incident CKD among individuals without CKD[11,13] and with the risk of CKD progression and kidney failure among those with CKD.[16–19,21,22] The present analysis expands these findings by demonstrating that: 1) longitudinal changes in NT–proBNP levels are also associated with subsequent changes in eGFR; 2) these findings appear particularly strong in those with prevalent CKD; and 3) baseline NT–proBNP and changes in NT–proBNP levels have prognostic value for kidney function decline regardless of the intensity of SBP lowering. The stronger associations in the CKD subgroup may be explained in part by higher baseline NT–proBNP levels and correspondingly greater absolute NT–proBNP changes. The NT–proBNP associations and interactions by CKD status were robust to adjustment for baseline and 1-year changes in eGFR, and similar interactions were observed in persons with and without albuminuria. The strength and consistency of these findings makes it unlikely that these findings are explained by chance, regression to the mean, or confounding by reduced NT–proBNP clearance in the setting of CKD.

Subclinical elevations in NT–proBNP may reflect chronic neurohormonal activation and venous congestion, which are mechanisms that can also contribute to the progression of kidney disease by impairing intrarenal blood flow.[32–34] However, the complex, bidirectional interplay between the heart and kidney and the reduced NT–proBNP excretion in the setting of CKD make it difficult to attribute an individual's elevated NT–proBNP level to a specific pathophysiological process. We recently demonstrated in SPRINT that intensive SBP lowering leads to greater reductions in NT–proBNP, and that this is primarily mediated by reductions in SBP.[28] Here we show that 1-year increases in NT–proBNP levels are associated with subsequent decreases in eGFR independent of treatment assignment and 1-year changes in SBP. Furthermore, we observed that decreases in NT–proBNP are associated with slower decreases in eGFR despite intensive SBP lowering having been shown to lead to decreased NT–proBNP levels and slightly faster decreases in eGFR.[5,6] Collectively, these results suggest that hemodynamic effects on NT–proBNP and eGFR do not fully explain our findings.

The results of this study suggest that longitudinal monitoring of NT–proBNP levels during hypertension treatment, particularly in those with CKD, may be useful for identifying individuals at higher risk for subsequent loss of kidney function. This builds upon previous work in SPRINT that showed individuals with higher baseline NT–proBNP levels derive greater benefit from intensive SBP lowering and that baseline NT–proBNP levels and changes in NT–proBNP over time provide prognostic information about the risks of heart failure and death during hypertension treatment.[27,28] Taken together, these data suggest a plausible role for routine NT–proBNP measurements during hypertension treatment to provide ongoing risk assessment of cardiorenal outcomes.

As an ancillary study of SPRINT, the present analysis benefited from the inclusion of a large cohort of individuals with and without CKD, repeated NT–proBNP measurements, and frequent and protocol-driven eGFR and BP assessments during follow-up. These data allowed us to evaluate the degree to which associations of dynamic changes in NT–proBNP levels with subsequent declines in eGFR were independent of concurrent changes in eGFR and SBP. There are also several limitations. Because of the SPRINT design, our findings may not generalize to persons with heart failure, diabetes mellitus, eGFR <20 mL/min/1.73 m^2, or severe proteinuria. In addition, the relatively short follow-up period of the trial precluded the evaluation of long-term changes in kidney function.

In summary, among individuals with hypertension without diabetes, higher baseline NT–proBNP levels and greater 1-year increases in NT–proBNP were associated with subsequent decreases in eGFR independent of baseline eGFR and albuminuria and regardless of the intensity of SBP lowering. These associations are particularly pronounced in persons with CKD. In the context of prior literature, these results advance the notion of considering NT–proBNP as a dynamic tool for assessing kidney disease risk dining hypertension treatment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Support:

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Data Sharing:

The data that support the findings of this study are available from the National Heart, Lung, and Blood Institute Biologic Specimen and Data Repositories and the corresponding author upon request.

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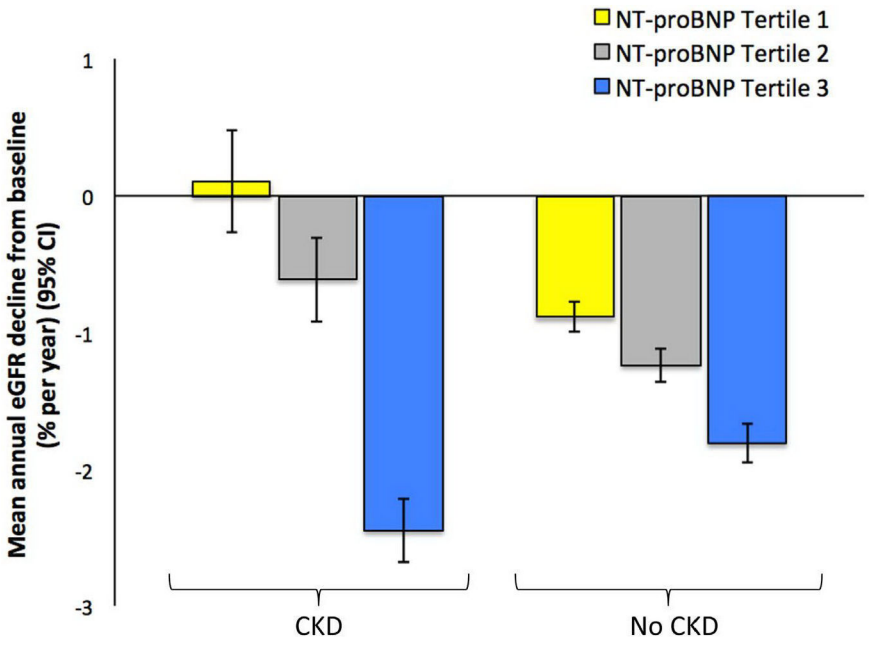

Figure 1.

Baseline tertiles of N-terminal pro–B-type natriuretic peptide (NT–proBNP) and subsequent kidney function decline. Bars represent unadjusted estimated annual change in estimated glomerular filtration rate (eGFR) from baseline with 95% CIs. Results were stratified by baseline chronic kidney disease (CKD) status. Estimates are derived from linear mixed-effect models.

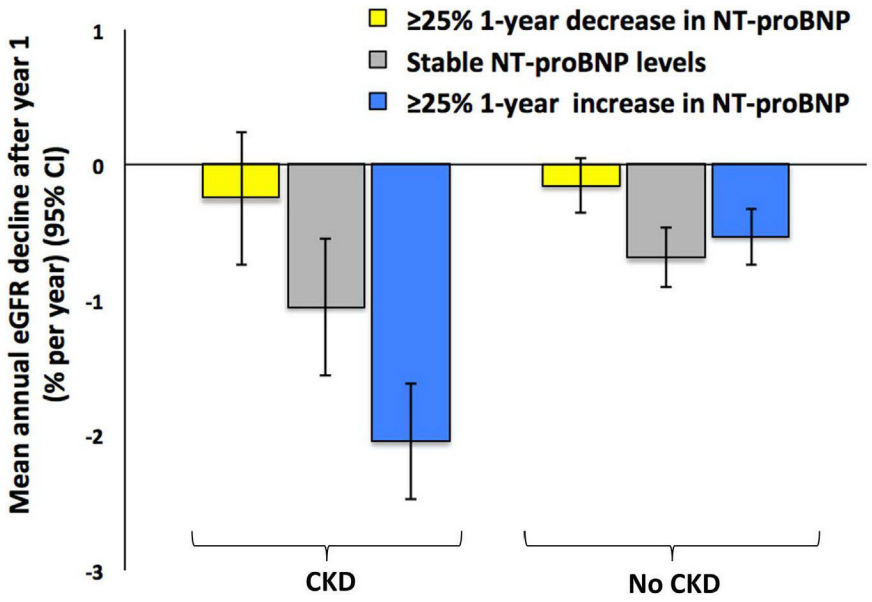

Figure 2.

Change in N-terminal pro–B-type natriuretic peptide (NT–proBNP) and subsequent kidney function decline. Bars represent unadjusted estimated annual change in estimated glomerular filtration rate (eGFR) from year 1 with 95% CIs. Results were stratified by baseline chronic kidney disease (CKD) status. Estimates are derived from linear mixed-effect models.

Table 1.

Baseline Characteristics of SPRINT Participants Stratified by 1-Year Changes in NT–proBNP

Characteristic	≥25% Increase in NT–proBNP (n = 2,804)	Stable NT–proBNP (n = 2,362)	≥25% Decrease in NT–proBNP (n = 2,839)	Total (N = 8,005)
Age, y	68 ± 9	70 ± 9	66 ± 9	68 ± 9
Female sex	986 (35%)	876 (37%)	1,039 (37%)	2,901 (36%)
Race				
White	1,692 (60%)	1,465 (62%)	1,553 (55%)	4,710 (59%)
Black	774 (28%)	605 (26%)	915 (32%)	2,294 (29%)
Hispanic	296 (11%)	250 (11%)	311 (11%)	857 (11%)
Smoking				
Current	1,230 (44%)	1,083 (46%)	1,268 (45%)	4,710 (59%)
Former	1,218 (44%)	1,046 (44%)	1,148 (41%)	2,294 (29%)
Never	353 (13%)	232 (10%)	420 (15%)	857 (11%)
Prevalent CVD	544 (19%)	493 (21%)	553 (20%)	1,590 (20%)
Prevalent heart failure	96 (3%)	78 (3%)	92 (2%)	266 (3%)
Systolic BP, mm Hg	137 ± 15	139 ± 15	143 ± 16	140 ± 16
Diastolic BP, mm Hg	77 ± 11	77 ± 11	80 ± 12	78 ± 12
No. of antihypertensive medications	1.9 ± 1.0	1.8 ± 1.1	1.8 ± 1.1	1.8 ± 1.0
Antihypertensive medication				
β-Blocker	925 (33%)	882 (37%)	1,120 (40%)	2,927 (37%)
Diuretic	1,373 (49%)	1,088 (46%)	1,244 (44%)	3,705 (46%)
Calcium channel blocker	1,054 (38%)	883 (37%)	871 (31%)	2,808 (35%)
ACEI or ARB	1,614 (58%)	1,290 (55%)	1,563 (55%)	4,467 (56%)
BMI, kg/m^2	29.9 ± 5.7	29.5 ± 5.5	30.1 ± 5.8	29.8 ± 5.7
eGFR, mL/min/1.73 m^2	73 ± 20	72 ± 19	75 ± 19	74 ± 19
eGFR <60 mL/min/1.73 m^2	757 (27%)	592 (25%)	609 (22%)	1,958 (24%)
Urine ACR, mg/g	9 [6–20]	10 [6–22]	10 [6–21]	10 [6–21]

Data displayed as mean ± standard deviation, n (%), or median [IQR] as appropriate.

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ACR, albumin-to-creatinine ratio; ARB, angiotensin receptor blocker; BMI, body mass index; BP, blood pressure; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate (based on creatinine); NT–proBNP, N-terminal pro–brain natriuretic peptide; SPRINT, Systolic Blood Pressure Intervention Trial.

Table 2,

Associations of Baseline NT–proBNP With Annualized eGFR Slope Stratified by Baseline CKD Status in SPRINT

		Annualized eGFR Slope, %/y (95% CI)	
Baseline NT–proBNP	**N**	**Mean**	**Adjusted Difference**
CKD			
Per 2-fold higher[a]	1,958	–1.37 (–1.54 to –1.20)	–0.44 (–0.56 to –0.33)
Tertile 1	371	0.10 (–0.27 to 0.48)	Reference
Tertile 2	571	–0.61 (–0.92 to –0.31)	–0.24 (–0.74 to 0.25)
Tertile 3	1,016	–2.45 (–2.68 to–2.21)	–1.38 (–1.90 to –0.87)
No CKD			
Per 2-fold higher	6,047	–1.24 (–1.31 to –1.17)	–0.10 (–0.14 to –0.05)
Tertile 1	2,357	–0.89 (–1.00 to –0.78)	Reference
Tertile 2	2,102	–1.24 (–1.36 to –1.12)	–0.10 (–0.27 to 0.07)
Tertile 3	1,588	–1.81 (–1.95 to–1.67)	–0.39 (–0.60 to –0.18)

Models adjust for age, sex, race/ethnicity, randomization arm, baseline cardiovascular disease, current smoking, body mass index, systolic blood pressure, diastolic blood pressure, number of antihypertensive medications, diuretic agent use, angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use, baseline eGFR, and urine albumin-creatinine ratio.

Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; NT–proBNP, N-terminal pro–B-type natriuretic peptide; SPRINT, Systolic Blood Pressure Intervention Trial.

[a] $P = 0.003$ for interaction by CKD status.

Table 3.

Associations of 1-Year Changes in NT–proBNP With Annualized eGFR Slope After Year 1 Stratified by Baseline CKD Status in SPRINT

		Annualized eGFR Slope After Year 1, %/y (95% CI)	
1-Year ΔNT–proBNP	**N**	**Mean**	**Adjusted Difference**
CKD			
≥25% decrease[a]	609	−0.25 (−0.74 to 0.24)	1.09 (0.35 to 1.83)
Stable	592	−1.05 (−1.56 to −0.55)	Reference
≥25% increase[b]	757	−2.05 (−2.48 to −1.62)	−1.04 (−1.72 to −0.36)
No CKD			
≥25% decrease	2,230	−0.16 (−0.36 to 0.04)	0.51 (0.21 to 0.81)
Stable	1,770	−0.69 (−0.91 to −0.47)	Reference
≥25% increase	2,047	−0.53 (−0.74 to −0.33)	0.12 (−0.18 to 0.42)

Models adjust for age, sex, race/ethnicity, randomization arm, baseline cardiovascular disease, current smoking, body mass index, diastolic blood pressure, number of antihypertensive medications used, diuretic agent use, angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker use, urine albumin-creatinine ratio, baseline NT–proBNP, baseline and 1-year change in systolic blood pressure, and year-1 and 1-year change in eGFR.

Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; NT–proBNP, N-terminal pro–B-type natriuretic peptide; SBP, systolic blood pressure; SPRINT, Systolic Blood Pressure Intervention Trial.

[a] $P = 0.4$ for interaction by CKD status comparing ≥25% decrease in NT–proBNP versus stable NT–proBNP.

[b] $P = 0.01$ for interaction by CKD status comparing ≥25% increase in NT–proBNP versus stable NT–proBNP.