HHS Public Access

Author manuscript

JACC Adv. Author manuscript; available in PMC 2024 May 02.

Published in final edited form as:

JACC Adv. 2024 February ; 3(2): . doi:10.1016/j.jacadv.2023.100775.

Change in Troponin I Levels With Intensive Blood Pressure Control:

A Post-Hoc Analysis of SPRINT

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Cardiac troponin (cTn) is a group of myocardial injury biomarkers used for diagnosing and prognosticating myocardial infarction.[1–3] Among the cTn subtypes, cTnI elevation is specific for myocardial damage, while cTnT elevation occurs in other conditions such as skeletal myopathies.[1–3] A previous study showed that cTnT levels increased with intensive systolic blood pressure (SBP) lowering in hypertensive individuals at 1 year, and a longitudinal increase in cTnT was associated with a higher risk of cardiovascular disease (CVD).[4] However, similar data on cTnI, a specific biomarker of myocardial injury, are lacking. This post-hoc analysis of the SPRINT (Systolic Blood Pressure Intervention Trial) aimed to assess the change in cTnI with intensive blood pressure (BP) control and the prognostic value of longitudinal changes in cTnI at 1 year for incident CVD.

Publicly available SPRINT data on the NHLBI BioLINCC was used for this study. Details of the SPRINT have been previously described.[4] hs-cTnI was measured on the Abbott i2000SR Immunochemistry Analyzer at Baylor College of Medicine using stored plasma samples collected at randomization and 1 year. The change in cTnI at 1 year was used to stratify the study population into ≥50% decrease, ≥50% increase, or unchanged (<50% change).[4] Change in cTnI was calculated by subtracting $\log_e$ ($cTnI_{randomization}$) from $\log_e$ ($cTnI_{1\text{-}year}$). The primary outcome was adjudicated CVD events (acute coronary syndrome, stroke, heart failure, or death from CVD). Continuous and categorical data were compared using the analysis of variance and the chi-square test, respectively. Geometric mean ratios for change in log cTnI with intensive BP lowering compared with standard treatment (SPRINT study arms) were estimated using multivariable adjusted linear regression models.[4] Cox models were used to assess the risk of the incident CVD after 1 year with the

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change in cTnI levels adjusted for age, sex, race, body mass index, baseline SBP, smoking, prevalent CVD, low-density lipoprotein cholesterol, statin use, left ventricular hypertrophy by electrocardiogram, estimated glomerular filtration rate (eGFR), change in eGFR at 1 year, site, treatment assignment, and baseline biomarker level.[4] Events within 1 year were censored.

Of the 8,011 participants having cTnI measurements at randomization and 1 year, the cTnI values decreased, did not change, and increased in 393 (4.9%), 6,442 (80.4%), and 1,176 (14.7%) participants at 1 year, respectively. A decrease in cTnI was associated with younger mean age [decreased cTnI group: 65.9 ± 8.9 years; unchanged cTnI group: 68.0 ± 9.4 years; and increased cTnI group: 68.0 ± 9.4 years; $P < 0.001$] and a larger decrease in mean SBP at 1 year (15.5 ± 22.5 mm Hg in decreased cTnI group vs 7.7 ± 19.8 mm Hg and 11.4 ± 19.6 mm Hg in the unchanged cTnI and increased cTnI groups, respectively; $P < 0.001$) but similar change in eGFR at 1 year (−1.6 ± 12.2 mL/min/1.73 m^2, −1.4 ± 11.1 mL/min/1.73 m^2, and −2.1 ± 12.9 mL/min/1.73 m^2 in decreased, unchanged, and increased cTnI groups, respectively; $P = 0.14$) Compared with the standard treatment group, ≥50% reduction in cTnI at 1 year was more common in the intensive treatment group (Figure 1). The intensive treatment group had a 7% decrease (geometric mean ratio: 0.93; 95% CI: 0.91-0.95; $P < 0.001$) in cTnI levels compared with the standard treatment group (Figure 1). Over a median follow-up of 3.3 (range: 2.8-3.8) years, there were 330 incident CVD events. The incidence rate for CVD was 12.7 (95% CI: 11.4-14.1) events per 1,000 person-years. An increase in log cTnI levels at 1 year was associated with a higher risk of incident CVD events (HR_{adj}: 1.67; 95% CI: 1.36-2.05).

In this post-hoc analysis of ~8,000 SPRINT participants, intensive BP reduction led to a decrease in cTnI levels compared with standard treatment. This decrease in cTnI remained significant irrespective of adjustment with changes in SBP, diastolic blood pressure, and eGFR. Increased cTnI levels at 1 year were associated with a higher risk of incident CVD and a composite of all-cause mortality or incident CVD. A prior SPRINT analysis showed that cTnT levels increased with intensive BP control (geometric mean ratio: 1.03; 95% CI: 1.01-1.04) and accounting for the change in eGFR at 1 year abolished this increase in cTnT levels (geometric mean ratio: 1.00; 95% CI: 0.99-1.02).[4] Lowering of eGFR is associated with an increase in cTnT levels but cTnI levels remain unaffected.[5] Additionally, cTnI has been shown to predict myocardial infarction and coronary heart disease, while cTnT has not.[1] A possible explanation for this discordance in the prognostic value of cTnT and cTnI in SPRINT may be attributed to the influence of eGFR on cTnT and noncardiac expression of cTnT.[2,5] Therefore, cTnT levels may lack specificity for prognostication compared with cTnI in the setting of changes in eGFR related to intensive BP control. cTnI represents an ideal cardiac-specific biomarker that is unaffected by eGFR alteration.[5] The current study findings of a decrease in cTnI levels with intensive BP reduction and the robust prognostic value of longitudinal changes in cTnI (irrespective of antihypertensive treatment) highlight the role of cTnI as a risk stratification marker. Furthermore, the longitudinal changes in cTnI can be used as a surrogate marker of the efficacy of an intervention. The cTnI changes can be used to monitor responses to preventive lifestyle measures, antihypertensives, and personalized treatment. This study is limited in evaluating the change in cTnI at 1 year and the exclusion of individuals with a CVD event within 1 year. To summarize, cTnI levels

decreased with intensive BP control, and the change in cTnI at 1 year predicted incident CVD events among individuals with elevated BP and an increased risk of CVD.

Acknowledgments

Dr Arora is supported by the National Heart, Lung, and Blood Institute of the National Institutes of Health (NIH) awards R01HL160982, R01HL163852, R01HL163081, and K23HL146887; has received grant support from Merck Sharp & Dohme LLC and Bristol-Myers Squibb; and has served as a consultant for Bristol-Myers Squibb (outside the submitted work). Dr Patel has served as a consultant for Novo Nordisk (outside the submitted work). All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. The authors thank the SPRINT Research Group for making the SPRINT data available on the National Heart, Lung, and Blood Institute Biologic Specimen and Data Repository Information Coordinating Center.

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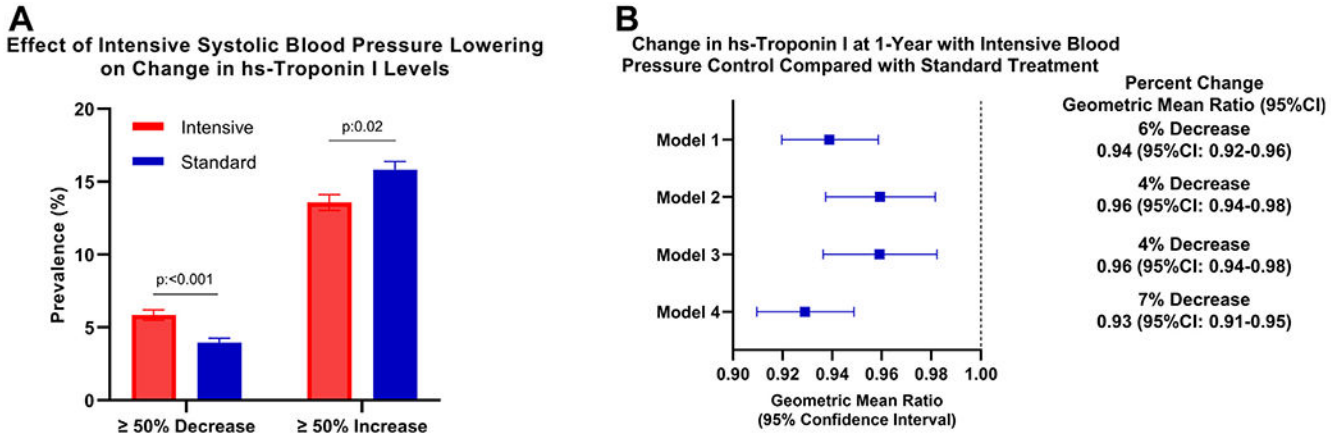

FIGURE 1. Change in hs-Troponin I at 1 Year With Intensive Systolic Blood Pressure Lowering

(A) Prevalence of a 50% increase and a 50% decrease in high-sensitivity troponin I (cTnI) after 1 year, according to study arms. (B) This figure depicts the geometric mean ratio of the change in high-sensitivity troponin I (cTnI) at 1 year with intensive blood pressure lowering compared with standard treatment, estimated using multivariable-adjusted linear regression models. The percentage change in cTnI levels was derived from the geometric mean ratio. Model 1 was adjusted for age, sex, race, BMI, baseline systolic blood pressure, diastolic blood pressure, smoking, prevalent cardiovascular disease, site, and baseline biomarker level. Model 2 was adjusted for the change in diastolic blood pressure at 1 year in addition to the covariates in Model 1. Model 3 was adjusted for the covariates in Model 2 and the change in systolic blood pressure. Model 4 was adjusted for the change in eGFR at 1 year in addition to the covariates in Model 3. BMI = body mass index; eGFR = estimated glomerular filtration rate.