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Effect of Intensive Blood Pressure Lowering on the Risk of Incident Silent Myocardial Infarction: A Post Hoc Analysis of a Randomized Controlled Trial

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According to a report by the American Heart Association, annually, 805,000 first and recurrent myocardial infarctions occur, with approximately 170,000 events being unrecognized or silent myocardial infarctions (SMI)

SMI is a well-established predictor of coronary heart disease , heart failure , sudden cardiac death , ischemic stroke, and mortality. A recent comprehensive meta-analysis found that SMI detected by ECG or cardiac magnetic resonance imaging (CMR) was associated with all-cause mortality and multiple CVD outcomes with risks comparable to those with RMI

Stroke (REGARDS) study found that participants with SMI were less likely than those with RMI to use aspirin, beta-blockers, statins, and angiotensin-convertingenzyme inhibitor

Individuals with RMI benefit from effective secondary preventive therapies to reduce this the risk of further cardiovascular events and mortality

CMR is a highly sensitive and specific modality to detect SMI and has consistently improved the prediction of CVD and mortality, while utilizing ECG to screen SMI has low sensitivity but high specificity .
Further, ECG may add additional predictive value for mortality and CVD events.

American Heart Association and American College of Cardiology consider ECG screening “reasonable” in asymptomatic individuals with hypertension or diabetes and stated that ECG “may be considered” in asymptomatic individuals without hypertension or diabetes
The 2021 European Society of Cardiology guidelines on cardiovascular prevention recommends a 12-lead ECG for all hypertensive individuals to detect hypertension-mediated organ damage (Class 1, Level B)

While routine CMR may be cost-prohibitive,
ECG surveillance of elderly individuals with hypertension and those at higher cardiovascular risk may be warranted as preventive strategies may reduce the risk of future SMI.
The increasing prevalence of SMI with age, with some reports suggesting the prevalence of SMI exceeds the prevalence of RMI with approximately 1–2 additional SMI for every RMI in the elderly population, further supports the consideration of screening for SMI in carefully selectedpopulations .

Further studies are needed to explore how to integrate ECG or imaging modalities to detect myocardial ischemia in such high-risk populations.

Hypertension is a major modifiable risk factor for ischemic heart disease, and clinical trials have shown approximately a 15%–25% reduction in the risk of MI with effective blood pressure (BP) control .

In the final report of the Systolic Blood Pressure Intervention Trial (SPRINT), intensive SBP control of less than 120 mmHg, compared to the standard goal of SBP of 140 mmHg, resulted in a 28% relative risk reduction of MI .

The adjudication of MI as a secondary endpoint in SPRINT included a combination of clinical RMI and SMI ascertained from electrocardiograms .

However, it is unknown if the effect of intensive BP control strategy would reduce the development of SMI. Therefore, we conducted a secondary analysis of the SPRINT with the hypothesis that intensive BP lowering would reduce the incidence and risk of SMI when compared to the standard BP control.

Sample (N=8,242)

- **Age 67.9±9.3 years**
- **35.2 % Female**
- **29.7% Black**
- **High-risk Hypertension**
- **No Diabetes Mellitus**

Standard Systolic BP Lowering (Target <140mmHg)

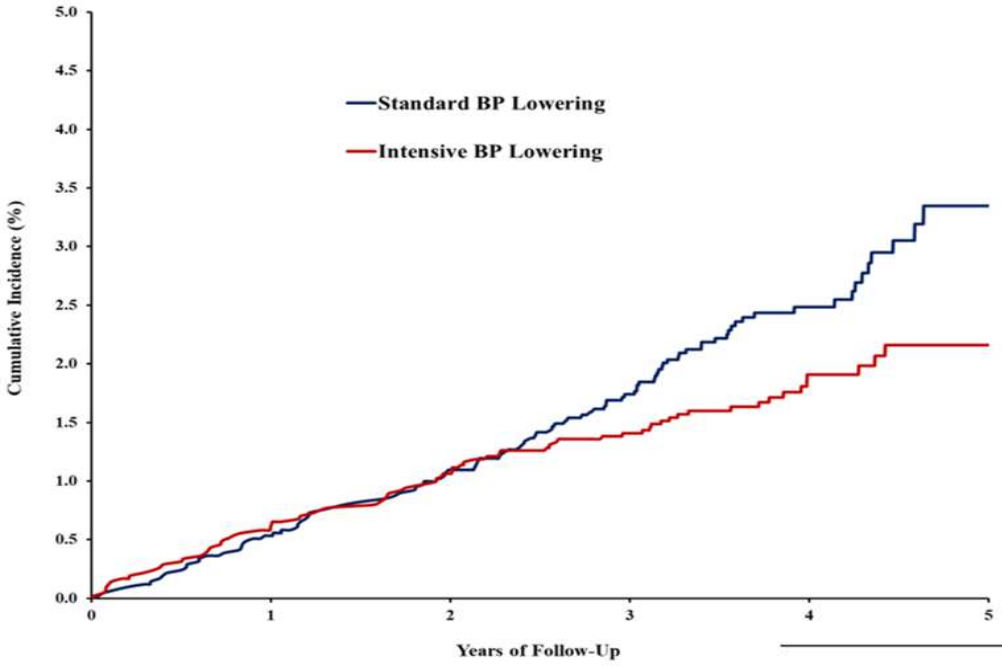
Intensive Systolic BP Lowering (Target <120mmHg)

High CVD risk was defined as ≥ 1
of the following:
- clinical or subclinical CVD,
- chronic kidney disease ,
- 10-year risk of CVD ≥ 15% by Framingham risk score,
- or age ≥ 75 years.

Clinical and laboratory data were obtained at baseline and every 3 months for the first year, then every 6 months for the next 4 years

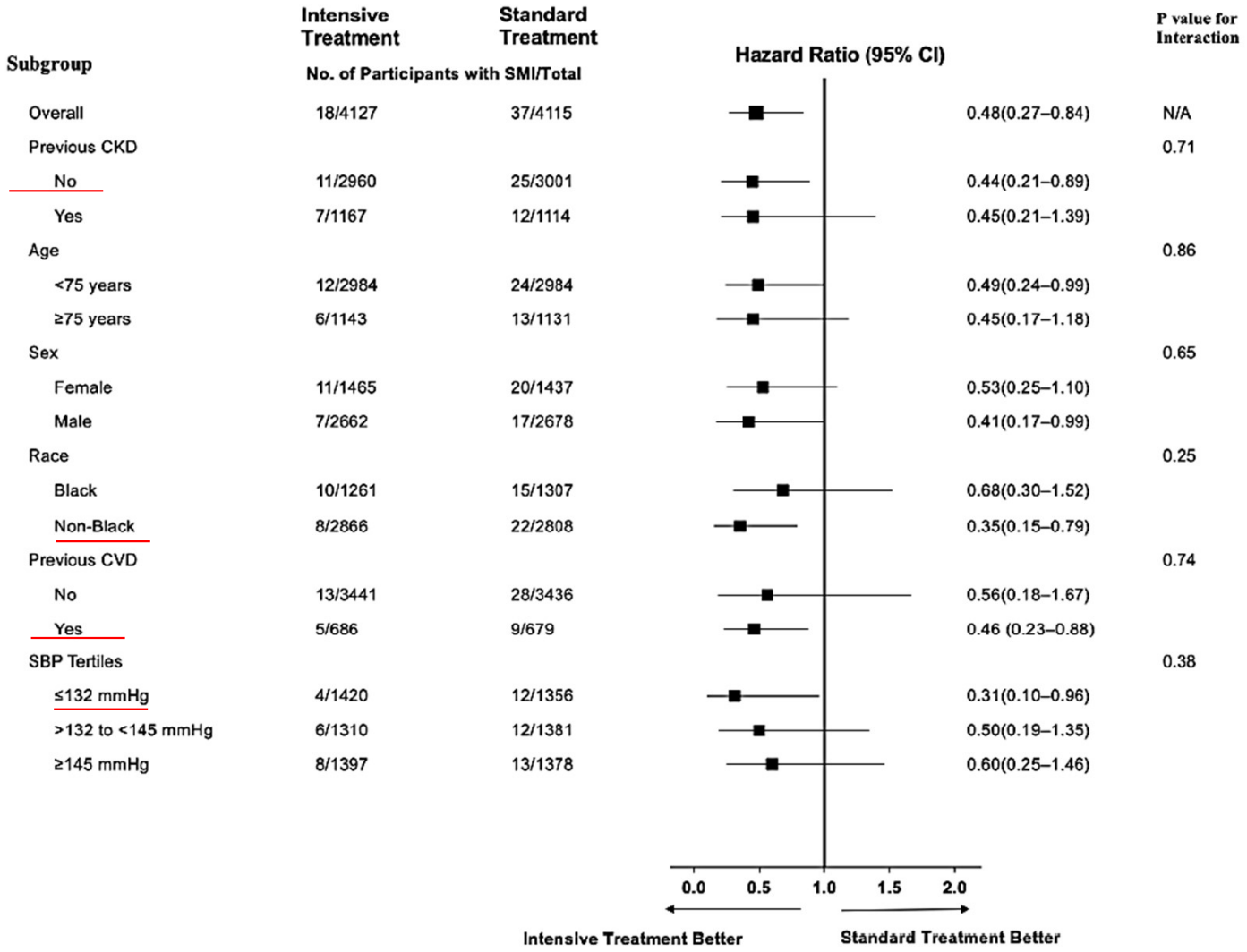
RMI was ascertained from the hospital records for clinical events using cardiac symptoms, biomarkers and ECG criteria. SMI, using 12-lead ECG at years 2 and 4 and the close-out
visit compared to baseline, was determined centrally as a finding of a new significant Q wave in the absence of clinical RMI

Characteristic mean ± SD, *n* (%) or median (IQR)	No MI (*N* = 8008)	RMI (*N* = 179)	SMI (*N* = 55)	*p*[a]	*p*[b]
Age, years	67.0 ± 9.3	71.6 ± 8.9	70.0 ± 9.2	0.252	< 0.001
Age ≥ 75 years	2180 (27.2)	75 (41.9)	19 (34.5)	0.331	< 0.001
Female	2828 (35.3)	43 (24.0)	31 (56.3)	< 0.001	< 0.001
Prior CKD	2195 (27.4)	67 (37.4)	19 (34.6)	0.698	0.006
Prior CVD	1546 (19.3)	76 (42.5)	15 (27.3)	0.043	< 0.001
Framingham 10-year CVD risk score	17.5 ± 10.6	26.4 ± 13.5	19.6 ± 11.4	0.001	< 0.001
Framingham risk ≥ 15%	4893 (61.1)	135 (75.4)	29 (52.7)	0.001	< 0.001
Race or ethnicity group					
Non-hispanic black	2390 (29.9)	31 (17.3)	23 (41.8)	0.002	0.003
Hispanic	838 (10.5)	17 (9.5)	3 (5.5)		
Non-hispanic white	4639 (57.9)	128 (71.5)	28 (50.9)		
Other	141 (1.8)	3 (1.7)	1 (1.8)		
Current smoker	1010 (12.6)	35 (19.6)	12 (21.8)	0.714	0.003
BMI, kg/m^2	29.1 ± 5.7	28.9 ± 5.1	29.4 ± 6.5	0.562	0.059
Systolic BP, mmHg	138.0 ± 15.5	140.9 ± 15.4	141.6 ± 16.7	0.762	0.300
Diastolic BP, mmHg	78.0 ± 11.8	74.5 ± 13.5	79.7 ± 12.8	0.012	< 0.001
SBP tertile					
≤ 132 mmHg	2705 (33.8)	55 (30.7)	16 (29.1)	0.814	0.790
> 132 to < 145 mmHg	2609 (32.6)	64 (35.8)	18 (32.7)		
≥ 145 mmHg	2694 (33.6)	60 (33.5)	21 (38.2)		
eGFR, mL/min per 1.73 m^2	71.5 ± 20.3	67.1 ± 20.8	68.1 ± 20.1	0.759	0.002
Creatinine, mg/dL	1.0 ± 0.3	1.1 ± 0.4	1.09 ± 0.36	0.377	0.007
UACR	9.4 (5.6–20.6)	14.9 (6.8–41.4)	12.1 (6.3–27.3)	0.278	< 0.001
Total cholesterol	187.0 ± 41.1	185.9 ± 43.4	188.5 ± 45.7	0.699	0.366
HDL, mg/dL	50.0 ± 14.4	49.2 ± 12.5	55.4 ± 14.5	0.002	0.001
Triglycerides, mg/dL, median	106 (77–150)	122.0 (87.0–157.0)	111.0 (69.0–155)	0.142	0.039
Fasting glucose, mg/dL	97.0 ± 13.5	98.4 ± 11.2	97.6 ± 13.2	0.650	0.698
Statin use	3480 (43.7)	107 (59.8)	25 (45.5)	0.0610	< 0.001
Aspirin use	4086 (51.1)	106 (61.2)	30 (54.6)	0.377	0.025
No. antihypertensive agents	2.0 ± 1.0	2.0 ± 1.0	2.2 ± 1.0	0.134	0.003



Treatment arm	Number of participants	Number of events	Events per 1000 person-years	HR (95% CI)	*p*	χ^2 *p* for MI subtyp difference[a]
Effect of intensive versus standard treatment on incident SMI						
Intensive	4127	18	1.1	0.48 (0.27–0.84)	0.01	0.23
Standard	4115	37	2.3			
Effect of intensive versus standard treatment on incident RMI						
Intensive	4127	75	4.6	0.71 (0.52–0.95)	0.02	
Standard	4115	104	6.5			

Effect of intensive blood pressure (BP) lowering on the risk of incident silent myocardial infarction (SMI)



Conclusion:

In hypertension, the benefit of intensive SBP lowering compared with standard SBP lowering, go beyond the prevention of recognized MI to include the prevention of SMI.

To the best of our knowledge, this is the first large trial in which the benefits of intensive BP control to reduce the risk of SMI are demonstrated.