

SUPPLEMENTAL MATERIAL

1. Supplemental Methods

A. Study 1: Discovery Cohort

Statins users were classified according to their LDL reduction capacity in three groups, no statin use (Group 1), low dose use (Group 2: atorvastatin 5 mg, lovastatin <20 mg, pravastatin <20 mg, simvastatin <10 mg and fluvastatin 20mg) or regular-high dose use (Group 3: atorvastatin \geq 10 mg, lovastatin \geq 40 mg, pravastatin \geq 40 mg, simvastatin \geq 20 mg and fluvastatin \geq 40 mg)¹.

In the regression model 1 in HyperPATH cohort, statin use effect was adjusted by age, BMI, gender, 24h urinary sodium (LS and HS) and including the effect of time (intervention points) in the model (1=HS baseline, 2=HS AngII stimulation, 3=LS baseline, 4=LS AngII stimulation). The second model included more potential confounders including those in model 1 plus race (Caucasian, African-American, Other), site (Boston, Salt Lake City, Paris) and intervention order (LS vs HS first). We also perform sensitivity analysis including LDL levels and systolic BP in the model (probably intermediary variables and not confounders). In order to test the robustness of the model we searched for effect measure modification introducing a priori interaction terms and tested for eventual collinearity

B) Study 2: Replication cohort

In the regression model 1 in the diabetes trial, aldosterone levels were adjusted by age, BMI, gender, and HS urinary sodium. In model 2, we included model 1 covariates plus race, T2DM duration and amlodipine use for hypertension control. Bootstrapping with 1000 iterations was performed to all regression models in both studies since this non-parametric methodology does not require normality assumptions, prevents false positive results by outliers and indicates our models were not over-fitted. Further analysis to check for residuals normality and non-linearity effect modification were performed.

1. Schachter M. Chemical, pharmacokinetic and pharmacodynamic properties of statins: An update. *Fundam Clin Pharmacol.* 2005;19:117-125

Supplementary Table. Baseline characteristics of diabetic participants categorized by statin use.

n=79	No Statin Group (21%)	Statin Group (79%)	p value
Age (years)	52.2 ± 8.9	54.2 ± 7.5	0.37
Female (%)	38	37	0.94
BMI (kg/m²)	32.9 ± 5.5	31.8 ± 4.4	0.37
Years of Diabetes	9.1 ± 7.6	7.6 ± 6.0	0.39
HS urinary sodium (24h mEq)	270.4 ± 90.2	272.3 ± 71.7	0.94
Aldosterone ng/dl (baseline)	4.18 ± 2.4	3.12 ± 1.1	0.01
Plasma renin activity (ng/mL*h)	2.89 ± 4.1	1.48 ± 2.5	0.19
Aldosterone ng/dl (AngII stim)	12.47 ± 7.8	9.22 ± 3.64	0.02
Cortisol ug/dL (baseline)	10.73 ± 3.6	10.09 ± 3.44	0.51

Data reported as mean ± SD, except as noted. HS indicates high sodium diet.

Supplementary Figure

Legend:

Aldosterone levels (mean \pm SD) categorized by statin use after sodium diet interventions and angiotensin II infusions in 317 hypertensive subjects from the HyperPATH protocol

