

Modulation of Plasma Sphingosine-1-phosphate Levels via Dietary Salt Intervention in Chinese Adults: An Intervention Trial

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Research

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Abstract

Background: Salt is a crucial factor for blood pressure modulation, especially in salt-sensitive individuals. Sphingosine-1-phosphate (S1P), a pleiotropic bioactive sphingolipid metabolite participating in blood pressure regulation, has recently been identified as a novel lipid diuretic factor. However, the relationships among salt intake, circulating S1P levels, and blood pressure changes in human beings are unknown. Thus, we conducted this intervention trial to explore the effect of dietary salt intake on plasma S1P levels and to examine the relationship between S1P and blood pressure in Chinese adults.

Methods: 42 participants (aged 18–65 years) were recruited from a rural community in Shaanxi, China. All participants first maintained their normal diet for 3 days, then sequentially ate a low-sodium diet (3.0 g/day NaCl) for 7 days, followed by a high-sodium diet (18.0 g/day NaCl) for 7 days. We assessed their plasma S1P concentrations on the last day of each intervention phase by liquid chromatography-tandem mass spectrometry. We classified the subjects who demonstrated at least a 10% increase in mean arterial pressure upon transitioning from a low-salt to a high-salt diet as salt-sensitive and the others as salt-resistant. Differences in repeated measures were analyzed by repeated-measures analysis of variance.

Results: Plasma S1P levels decreased significantly from the baseline to low-salt diet period and increased from the low-salt to high-salt diet period. We observed this response in both salt-sensitive and salt-resistant individuals. Plasma S1P levels positively correlated with 24-hour urinary sodium excretion, but not 24-hour urinary potassium excretion. In line with plasma S1P level responses to salt intervention, systolic blood pressure (SBP) and mean arterial pressure (MAP) decreased from the baseline to low-salt diet period and increased from the low-salt to high-salt period. SBP positively correlated with plasma S1P and the correlation was stronger in salt-sensitive individuals than that in salt-resistant individuals.

Conclusion: Low-salt dietary intervention decreases plasma S1P levels, whereas high-salt intervention reverses this change and S1P levels positively correlated with SBP in Chinese adults. This provides a high-efficiency and low-cost intervention for plasma S1P levels modulation, with implications for salt-induced blood pressure modulation.

Trial registration: NCT02915315. Registered 27 September 2016, <http://www.clinicaltrials.gov>

Introduction

Sphingosine-1-phosphate (S1P) is a bioactive sphingolipid metabolite and regulates the functions of multiple systems, such as the immune system, central nervous system, and cardiovascular system [1–3]. Its signaling pathway contributes to cardiac remodeling and protects cardiomyocytes from hypoxic and ischemia/reperfusion injury [4–6]. Also, a growing body of literature suggests that it plays an essential role in vascular endothelial and smooth muscle cell functions, through which it modulates vascular tone and blood pressure (BP) [7–9]. Thus, manipulation of S1P signaling pathway will offer new therapeutic approaches to cardiovascular diseases.

Several pharmacological S1PR agonists and antagonists are available. They serve as important tools for targeting different cells and systems. Cantalupo et al. found that the S1PR1 selective agonist SEW2871 restores normal BP in hypertensive mice [10]. The administration of FTY720, a modulator of S1PRs, for a period of 10 days raised the BP of rats in a dose-dependent manner, whereas a single dose of FTY720 further increased the BP of spontaneously hypertensive rats at 24 hours post-administration [11, 12]. However, the levels of circulating S1P are relatively high (0.1–1 μ M) compared to the potency of S1P on S1PR [13] and there are no simple and effective approaches to regulate circulating S1P levels. Only a few studies have focused on the effects of circulating S1P on BP modification using in vivo models, with controversial results. Generation of S1P in response to anandamide reduce mean arterial pressure in mice [14], but Forrest et al. found that continuous infusion of S1P was predominantly associated with an increase in BP in both rats and mice [15]. It's quite necessary to find a simple and effective way to regulate circulating S1P levels and to explore the relationship between S1P and blood pressure in human.

Salt intake is thought to be the most critical environmental factor for BP regulation. Nearly one-half of essential hypertensive patients have salt sensitivity [16], which is accompanied by risk of earlier, more severe target organ damage [17]. Many studies have demonstrated that salt overload strongly contributes to the development and progression of hypertension [18], whereas salt restriction plays an essential role in BP control and is recommended by guidelines worldwide [19–21]. Notably, S1P has recently been identified as a novel lipid diuretic factor that participates in sodium metabolism in the renal medulla [22]. This evidence emphasizes a possible role for S1P in the response to salt intervention and salt-induced BP change.

Thus, we conducted this study to investigate whether plasma S1P responds to salt intervention in Chinese adults and to examine the relationship between S1P levels and BP to identify a potential intervention for regulating circulating S1P levels and a novel target to determine the mechanism of salt-induced BP change.

Methods

2.1 Patient selection

72 permanent residents (aged 18–65 years) with similar dietary habits were recruited from a rural community in Shaanxi, China. We used a standard questionnaire administered by professional staff to collect basic demographic information (age, sex, education, ethnicity, occupation, physical activity, cardiovascular disease-related history, and physical examination findings). Hypertension was defined as systolic BP (SBP) \geq 140 mmHg and/or diastolic BP (DBP) \geq 90 mmHg, and/or a history of hypertension with current use of anti-hypertensive medications.

The exclusion criteria included: stage 2 hypertension; secondary hypertension; history of cardiovascular disease, chronic liver disease, chronic kidney disease, or diabetes; pregnancy; mental disorder and alcohol abuse. Finally, 42 subjects met the inclusion criteria and participated in this study (Fig. 1) .

This study was performed in accordance with the Declaration of Helsinki and was approved by the ethics committee of the First Affiliated Hospital of Medical School, Xi'an Jiaotong University (Code: 2015 – 128). All participants provided signed informed consent. The trial registration number was NCT02915315 (<http://www.clinicaltrials.gov>), with a date of registration of 27 September, 2016.

2.2 Dietary salt intervention and physical examination

The dietary intervention included a 3-day baseline diet characterized by habitual salt intake, followed by a 7-day low-salt intervention (51.3 mM sodium or 3.0 g NaCl per day), and then a 7-day high-salt intervention (307.8 mM sodium or 18.0 g NaCl per day). Prepacked salt was added to salt-free meals cooked by the study kitchen; participants ate their breakfast, lunch, and supper under the supervision of professional staff during the whole intervention period to ensure compliance with the intervention protocol. Any food that was not provided by study personnel was forbidden. Physical examinations, including height, weight, and waist circumference measurements, were conducted twice on the last day of each period. We measured brachial-ankle artery pulse wave velocity at the same time.

2.3 BP measurement and salt sensitivity definition

BP was measured by certified physicians using standard mercury sphygmomanometers according to the protocol recommended by the American Heart Association. Participants were instructed to sit in a resting position for more than 5 minutes after avoiding exercise; smoking; and alcohol, coffee, or tea consumption for at least 30 minutes before BP measurement. BP was measured 3 times at 1-minute intervals on each day of baseline observation and on the last 2 days of the low- and high-salt intervention periods; we recorded the mean value. The BP of each participant was measured by the same physician using the same sphygmomanometer to avoid observation variation. Mean arterial pressure (MAP) was calculated as $MAP = (SBP/3) + (DBP \times 2/3)$. Due to the lack of an authoritative consensus on the definition of salt sensitivity based on BP, we classified subjects who demonstrated at least a 10% increase in MAP between the low-salt and high-salt diets as salt-sensitive (SS) and the others as salt-resistant (SR) [23].

2.4 Biochemical analyses

Blood samples were obtained by venipuncture on the last morning of each intervention phase. Within 2 hours of collection, staff centrifuged the samples at $3,000 \times g$ for 10 min to separate EDTA plasma and serum, which were shipped to a central laboratory via standardized procedures where they were stored at $-80\text{ }^{\circ}\text{C}$ until further analysis. We measured serum creatinine, uric acid, fasting serum glucose, total cholesterol, triglyceride, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol levels using an automatic biochemical analyzer (model 7600; Hitachi, Tokyo, Japan).

2.5 Plasma S1P detection

We used a previously described protocol to measure plasma S1P levels by liquid chromatography-tandem mass spectrometry [24].

2.6 24-hour urinary sodium and potassium determination

We collected 24-hour urine samples on the last day of each period, which we froze at $-40\text{ }^{\circ}\text{C}$ until further analysis. We determined the urinary concentrations of sodium and potassium using ion-selective electrodes (Hitachi, Tokyo, Japan). The 24-hour urinary excretion of sodium and potassium were calculated as 24-hour excretion = $[\text{Na}^+ \text{ or } \text{K}^+] \times 24\text{-hour total urine volume}$.

2.7 Statistical analysis

We performed statistical analyses with SPSS Statistics 22.0 (IBM, Chicago, IL, USA). Continuous data are presented as the mean \pm standard deviation. Categorical data are shown as frequency and percentage. Differences in repeated measures were analyzed by repeated-measures analysis of variance. Differences in characteristics between the SS and SR groups were analyzed by independent t-tests for continuous variables, where appropriate; they were otherwise analyzed by Mann–Whitney U test. We determined correlations by calculating Pearson's correlation coefficient, where the residuals were normally distributed, and by calculating Spearman's correlation coefficient in other cases. A two-tailed P-value ≤ 0.05 was considered statistically significant.

Results

3.1 Baseline characteristics of subjects

The basic characteristics of the subjects are outlined in Table 1. Of the 42 recruited subjects, 12 (28.6%) were classified as SS and the other 30 subjects (71.4%) were defined as SR individuals who showed little or no response to salt loading. No significant differences were found in age, body mass index, or BP between the SS and SR groups. However, the prevalence of hypertension (50% versus 16.7%, $p = 0.026$), glucose levels ($5.82 \pm 0.71\text{ mM}$ versus $5.21 \pm 0.70\text{ mM}$, $p = 0.015$), and brachial-ankle pulse wave velocity ($1665.08 \pm 392.49\text{ cm/s}$ versus $1402.10 \pm 200.26\text{ cm/s}$, $p = 0.045$) in SS subjects were significantly higher than in SR subjects (Table 1).

Table 1
Baseline Characteristics of Subjects

Parameters	Overall	Salt-Resistant Subjects	Salt-Sensitive Subjects
N(%)	42	30(71.4%)	12(28.6%)
Age, years	51.8 ± 12.3	50.1 ± 13.7	56.4 ± 9.2
Body mass index, kg/m ²	24.86 ± 3.22	24.56 ± 3.14	25.62 ± 3.43
Smoking, n (%)	5(5.7%)	5(16.7%)	0
Hypertension, n (%)	11(26.2%)	5(16.7%)	6(50.0%)*
SBP, mmHg	126.2 ± 18.3	123.8 ± 16.3	131.2 ± 22.2
DBP, mmHg	80.7 ± 9.7	81.5 ± 9.4	83.3 ± 10.9
MAP, mmHg	95.9 ± 11.4	95.4 ± 10.8	99.3 ± 14.0
Glucose, mmol/L	5.38 ± 0.75	5.21 ± 0.70	5.82 ± 0.71*
Total cholesterol, mmol/L	4.58 ± 0.90	4.59 ± 0.89	4.58 ± 0.94
Triglycerides, mmol/L	1.38 ± 0.81	1.13 ± 0.59	1.42 ± 0.62
LDL, mmol/L	2.56 ± 0.66	2.53 ± 0.60	2.64 ± 0.83
HDL, mmol/L	1.48 ± 0.42	1.51 ± 0.45	1.40 ± 0.33
Uric acid, μmol/L	256.07 ± 72.08	268.33 ± 70.97	225.42 ± 68.21
Serum creatinine, μmol/L	52.17 ± 7.26	51.64 ± 8.08	50.43 ± 5.38
BaPWV, cm/s	1477.24 ± 290.09	1402.10 ± 200.26	1665.08 ± 392.49*
Values are presented as mean ± SD. Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; LDL, low-density lipoprotein; HDL, high-density lipoprotein; BaPWV, brachial-ankle pulse wave velocity.* p < 0.05 vs Salt-resistant subjects.			

3.2 Effects of dietary salt intervention on BP and 24-hour urinary sodium and potassium excretion

Sodium excretion in 24-hour urine is a reliable indicator of salt intake; we collected 24-hour urine on the last day of each period. We found that 24-hour urinary sodium excretion decreased significantly from the baseline to low-salt intervention period in all groups (whole cohort: 167.5 ± 89.7 mM/24 h versus 72.6 ± 28.1 mM/24 h, $p < 0.001$; SS group: 159.2 ± 120.7 mm/24 h versus 73.6 ± 22.2 mM/24 h, $p = 0.034$; and SR group: 178.0 ± 76.6 mM versus 68.2 ± 32.9 mM/24 h, $p = 0.004$). From the low-salt to high-salt intervention period, 24-hour urinary sodium excretion increased (whole cohort: 72.6 ± 28.1 mm//24 h versus 302.1 ± 88.3 mM/24 h, $p < 0.001$; SS group: 73.6 ± 22.2 mM/24 h versus 297.9 ± 61.5 mM/24 h, $p < 0.001$; and SR group: 68.2 ± 32.9 mM/24 h versus 312.3 ± 106.4 mM/24 h, $p < 0.001$). These findings demonstrate that the subjects complied well with the dietary intervention protocol. Conversely, the 24-

hour urinary potassium excretion did not change between the baseline and low-salt periods. It increased from the low-salt to high-salt period in the whole cohort (24.5 ± 9.4 mM/24 h versus 36.0 ± 11.2 mM/24 h, $p = 0.003$) and the SR group (24.3 ± 9.8 mM/24 h versus 39.1 ± 12.2 mM/24 h, $p = 0.049$), but not in the SS group.

In line with the changes in urinary sodium excretion, we observed decreases in SBP and MAP from the baseline to low-salt period (SBP: 126.2 ± 18.3 mmHg versus 117.7 ± 13.7 mmHg, $p < 0.001$; MAP: 95.9 ± 11.4 mmHg versus 91.3 ± 8.0 mmHg, $p = 0.035$) and increases from the low-salt to high-salt period (SBP: 130.7 ± 20.3 mmHg versus 117.7 ± 13.7 mmHg, $p < 0.001$; MAP: 91.3 ± 8.0 mmHg versus 97.7 ± 10.7 mmHg, $p < 0.001$) in the whole cohort. The SBP, DBP, and MAP of SS individuals significantly increased from the low-salt to high-salt period (SBP: 148.4 ± 19.6 mmHg versus 123.9 ± 15.2 mmHg, $p < 0.001$; DBP: 87.2 ± 6.1 mmHg versus 79.9 ± 5.8 mmHg, $p < 0.001$; and MAP: 107.6 ± 9.7 mmHg versus 94.6 ± 7.9 mmHg, $p < 0.001$). The readings of the SS individuals were much higher than those of the SR individuals in the high-salt period (SBP: 148.4 ± 19.6 mmHg versus 121.8 ± 14.2 mmHg, $p = 0.002$; DBP: 107.6 ± 9.7 mmHg versus 92.8 ± 7.4 mmHg, $p = 0.001$; and MAP: 87.2 ± 6.1 mmHg versus 78.3 ± 6.6 mmHg, $p = 0.008$, respectively) (Table 2).

Table 2
Blood pressure and 24-h urinary sodium and potassium excretion at baseline and during dietary intervention period

	SBP, mmHg	DBP, mmHg	MAP, mmHg	Urinary Na ⁺ , mmol/24 h	Urinary K ⁺ , mmol/24 h
Overall					
Baseline	126.2 ± 18.3	80.7 ± 9.7	95.9 ± 11.4	167.5 ± 89.7	25.0 ± 9.9
LS	117.7 ± 13.7 ^{aaa}	78.1 ± 7.1	91.3 ± 8.0 ^a	72.6 ± 28.1 ^{aaa}	24.5 ± 9.4
HS	130.7 ± 20.3 ^{bbb}	81.2 ± 7.6 ^b	97.7 ± 10.7 ^{bbb}	302.1 ± 88.3 ^{aaabbbb}	36.0 ± 11.2 ^{aabb}
SS subjects					
Baseline	131.2 ± 22.2	83.3 ± 10.9	99.3 ± 14.0	159.2 ± 120.7	20.6 ± 11.3
LS	123.9 ± 15.2	79.9 ± 5.8	94.6 ± 7.9	73.6 ± 22.2 ^a	21.8 ± 8.5
HS	148.4 ± 19.6 ^{abbbb**}	87.2 ± 6.1 ^{bbb**}	107.6 ± 9.7 ^{bbb**}	297.9 ± 61.5 ^{bbb}	33.5 ± 10.1
SR subjects					
Baseline	123.8 ± 16.3	79.4 ± 9.2	94.2 ± 10.1	178.0 ± 73.6	28.0 ± 8.3
LS	114.6 ± 12.4 ^{aa}	77.3 ± 7.7	89.7 ± 7.8	68.2 ± 32.9 ^{aa}	24.3 ± 9.8
HS	121.8 ± 14.2 ^{bbb}	78.3 ± 6.6	92.8 ± 7.4 ^b	312.3 ± 106.4 ^{aaabbbb}	39.1 ± 12.2 ^b
<p>Values are presented as mean ± SD. ^a p < 0.05 versus baseline, ^{aa} p < 0.01 versus baseline, ^{aaa} p < 0.001 versus baseline. ^b p < 0.05 versus low-salt diet, ^{bb} p < 0.01 versus low-salt diet, ^{bbb} p < 0.001 versus low-salt diet. ^{**} p < 0.01 versus Salt-resistant individuals. Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; LS, low-salt; HS, high-salt; SS, salt-sensitive; SR, salt-resistant.</p>					

3.3 Effects of dietary salt intervention on plasma S1P levels

Plasma S1P levels decreased significantly from the baseline period to low-salt diet period and increased from the low-salt to high-salt period in the whole cohort (baseline: 1.455 ± 0.390 μM, low-salt period: 1.017 ± 0.245 μM, and high-salt period: 1.395 ± 0.288 μM). Further analysis revealed that S1P levels showed the same trend in the SS group (baseline: 1.278 ± 0.255 μM, low-salt period: 0.849 ± 0.197 μM, and high-salt period: 1.294 ± 0.164 μM) and the SR group (baseline: 1.542 ± 0.423 μM, low-salt period: 1.101 ± 0.228 μM, and high-salt period: 1.445 ± 0.328 μM). However, the plasma S1P level during the low-salt period in the SS group was significantly lower than that in the SR group, with no significant

differences during the baseline and high-salt periods (low-salt period SS: $0.849 \pm 0.197 \mu\text{M}$ versus low-salt period SR: $1.101 \pm 0.228 \mu\text{M}$, $p = 0.022$) (Fig. 2).

3.4 Correlations

S1P levels positively correlated with 24-hour urinary sodium excretion in the whole, SS, and SR group ($r = 0.416$, $p = 0.001$; $r = 0.566$, $p = 0.007$; and $r = 0.328$, $p = 0.036$, respectively), but not with 24-hour urinary potassium excretion ($r = 0.145$, $p = 0.261$; $r = 0.233$, $p = 0.310$; and $r = 0.007$, $p = 0.963$, respectively) (Fig. 3).

We observed a positive correlation between S1P levels and SBP in the whole, SS, and SR groups ($r = 0.290$, $p = 0.021$; $r = 0.762$, $p < 0.001$; and $r = 0.350$, $p = 0.023$, respectively); the correlation reached a higher level of statistical significance in the SS individuals than in the SR individuals. Further analysis revealed that S1P levels also positively correlated with MAP and DBP in SS individuals ($r = 0.707$, $p < 0.001$ and $r = 0.612$, $p = 0.003$, respectively) but not in SR individuals ($r = 0.271$, $p = 0.082$ and $r = 0.127$, $p = 0.421$, respectively) (Fig. 4).

Discussion

This is the first study to reveal that low-salt dietary intervention decreases plasma S1P levels, whereas high-salt intervention reverses that change, in SS and SR Chinese adults. The positive correlations between plasma S1P levels and SBP, MAP and 24-hour urinary sodium excretion, but not 24-hour urinary potassium excretion indicate that plasma S1P levels are responsive to dietary salt intervention and that circulating S1P levels may be involved in salt-sensitive blood pressure regulation. It provides a high-efficiency, low-cost, non-pharmaceutical approach to regulating circulating S1P levels and suggests that circulating S1P and its signaling pathway may be involved in salt-sensitive blood pressure regulation.

S1P and its signaling pathway contributes to the pathogenesis of a broad range of diseases, including atherosclerosis, pulmonary arterial hypertension, diabetes mellitus, and cancer [25–28]. Patients who experience pre-infarction angina have higher serum S1P levels than patients without pre-infarction angina [29], and ST segment elevation myocardial infarction patients have low plasma S1P concentrations and an accumulation of free sphingoid bases and their 1-phosphates in their erythrocytes [30], supporting the hypothesis that S1P mediates important cardiovascular protective functions. It is of great significance to maintain S1P levels in these patients. However, Ardawi et al. found that plasma S1P levels were significantly higher in women with incident fracture than in those without osteoporosis-related fractures, and high S1P levels were strongly associated with increased fracture risk [31]. Decreasing circulating S1P levels to physiological levels will certainly benefit those patients. In our study, a low-salt intervention for 7 days decreased plasma S1P levels and a high-salt intervention for 7 days reversed the change, suggesting that dietary salt intervention is a highly efficient and low-cost approach to regulate circulating S1P levels. The fact that circulating S1P is synthesized and degraded rapidly under the regulation of a specific enzyme may explain why a short-term intervention was able to statistically decrease plasma S1P

levels. We also find that S1P levels positively correlated with 24-hour urinary sodium excretion but not with 24-hour urinary potassium excretion, revealing that it is sodium but not potassium that modulates S1P levels.

A growing number of studies have shown that S1P and its signaling pathway may participate in BP regulation and hypertension [32–34]. The effect of S1P on BP is the result of changes in both vascular and heart functions. S1PR1 and S1PR3 are expressed in the heart [35]; S1PR1 and S1PR3 in the endothelium mediate vasodilation, resulting in lower BP, whereas S1PR2 and S1PR3 in smooth muscle mediate vasoconstriction, resulting in higher BP [7–9, 36]. As the first study to examine the relationship between S1P and blood pressure in human being, we observed a positive correlation between S1P levels and SBP in both SS and SR groups, providing important evidence for S1P research. Notably, the correlation was stronger in SS individuals than that in SR individuals and S1P levels positively correlated with MAP and DBP in SS individuals but not in SR individuals. Also, the plasma S1P levels in SS individuals were lower than those in SR individuals, with statistical significant differences during the low-salt period. These results demonstrate a potential role for S1P in mediating salt sensitivity and salt-induced BP change. In fact, EDG1 (also known as S1P1R) is a candidate for the control of salt sensitivity and hypertension in the stroke-prone spontaneously hypertensive rat model [37]. Zhu et al. found that S1P is a novel lipid diuretic factor in the renal medulla [22]. S1P produced NO-independent natriuretic effects by inhibiting ENaC activity via S1P1R to inhibit sodium reabsorption in the collecting tube and to increase urinary sodium excretion [22]. In accordance with those findings, our study verified a positive correlation between plasma S1P levels and 24-hour urinary sodium excretion. Taken together with the literature, our results indicate that S1P is responsive to dietary salt intervention and may be involved in determining salt sensitivity and BP regulation. Therefore, it constitutes a novel target for studying salt sensitivity and salt-induced hypertension.

One limitation of our study is the small number of participants recruited from Northern China. Large, multiethnic clinical trials should be conducted to determine if the results of our study can be generalized to diverse populations. Moreover, further studies should be conducted to explore the underlying mechanism of salt-induced plasma S1P changes and to investigate the interaction between S1P and BP.

Conclusions

Low-salt dietary intervention decreases plasma S1P levels, whereas high-salt intervention reverses this change and S1P levels positively correlated with SBP, in Chinese adults. Further studies will determine if this high-efficiency, low-cost intervention approach is suitable for regulating circulating S1P levels in diverse populations. We expect that S1P regulates salt-induced BP changes and represents a potential target for treating salt-induced hypertension.

Abbreviations

S1P

Sphingosine-1-phosphate

S1PR

Sphingosine-1-phosphateReceptor

BP

Blood Pressure

SBP

Systolic Blood Pressure

DBP

Diastolic Blood Pressure

MAP

Mean Arterial Pressure

LS

Low-salt

HS

High-salt

SS

Salt-sensitive

SR

Salt-resistant

EDTA

High-density Lipoprotein

HDL

High-density Lipoprotein

LDL

Low-density Lipoprotein

baPWV

Brachial-ankle Pulse Wave Velocity

SD

Standard Deviation

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the ethics committee of the First Affiliated Hospital of Xi'an Jiaotong University (Code: 2015-128). All participants provided written informed consent. All steps of the study conformed to the Helsinki Declaration.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Conceived and designed the experiments: JM CC QM. Performed the experiments: QM CC YX JH WZ YY KW YY YL CC. Analyzed the data: QM. Contributed reagents/materials/analysis tools: QM YX. Wrote the paper: QM. The author(s) read and approved the final manuscript.

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Not applicable

Acknowledgements of conflicts of interest: None.

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Figures

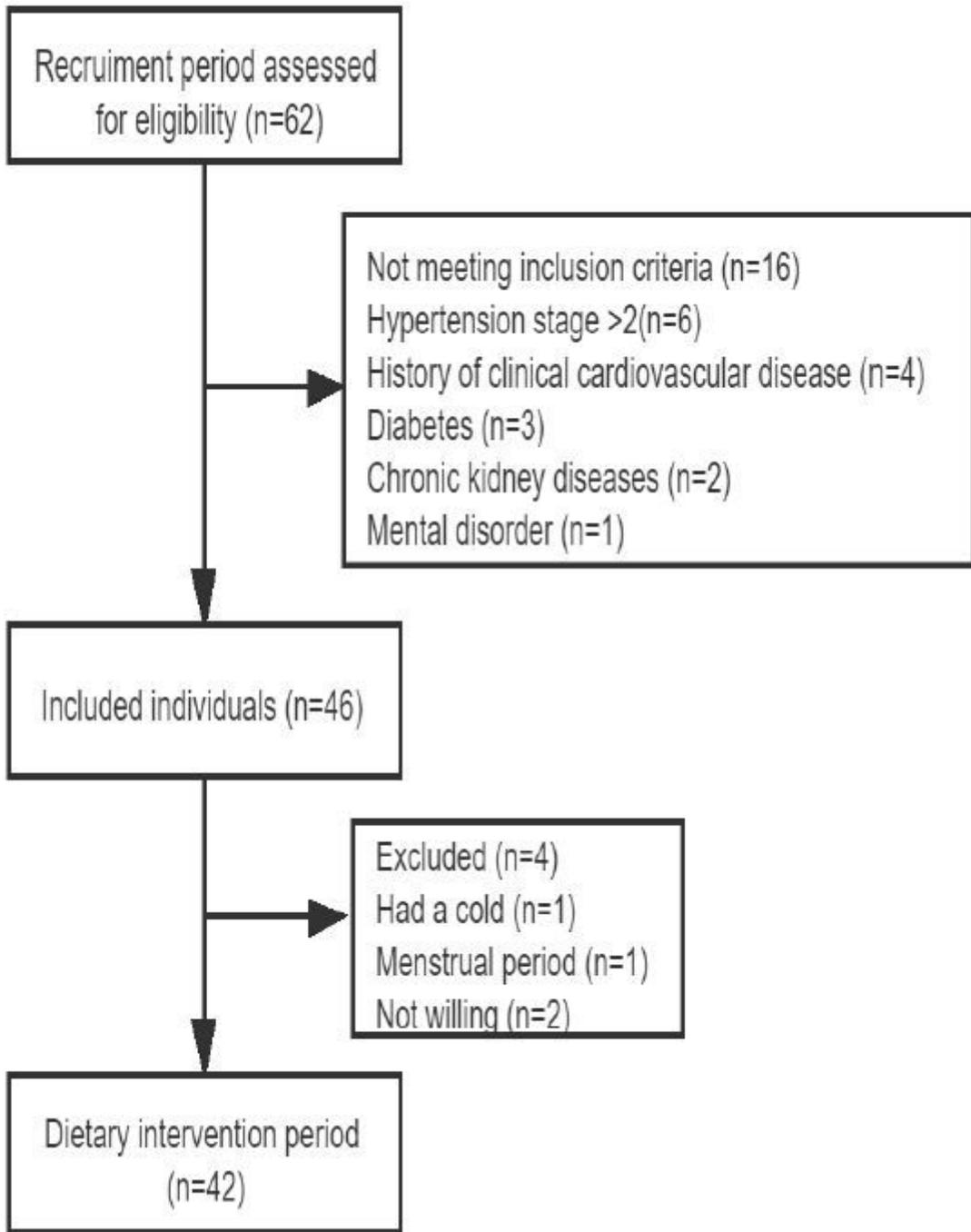


Figure 1

Flow diagram for study participants

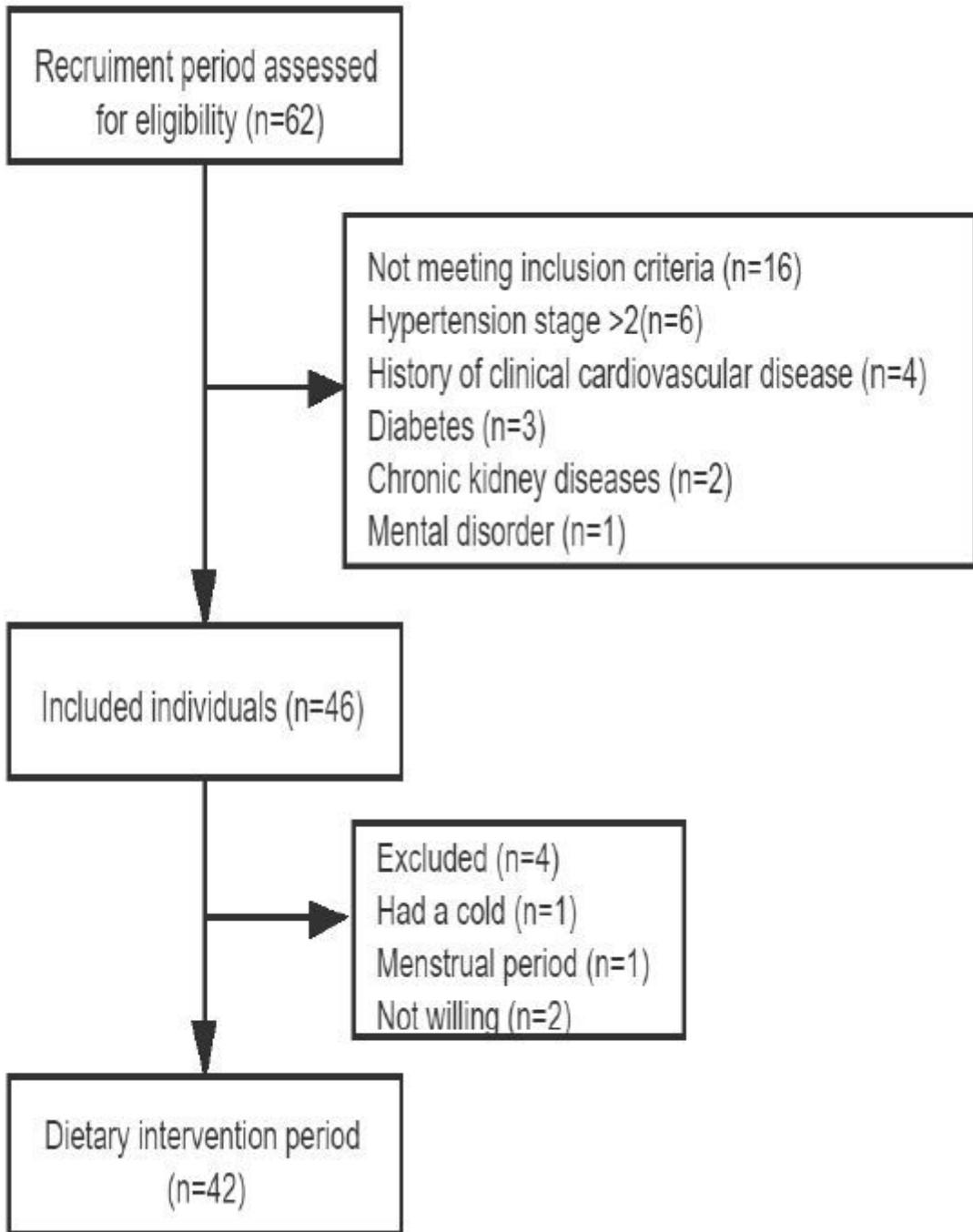


Figure 1

Flow diagram for study participants

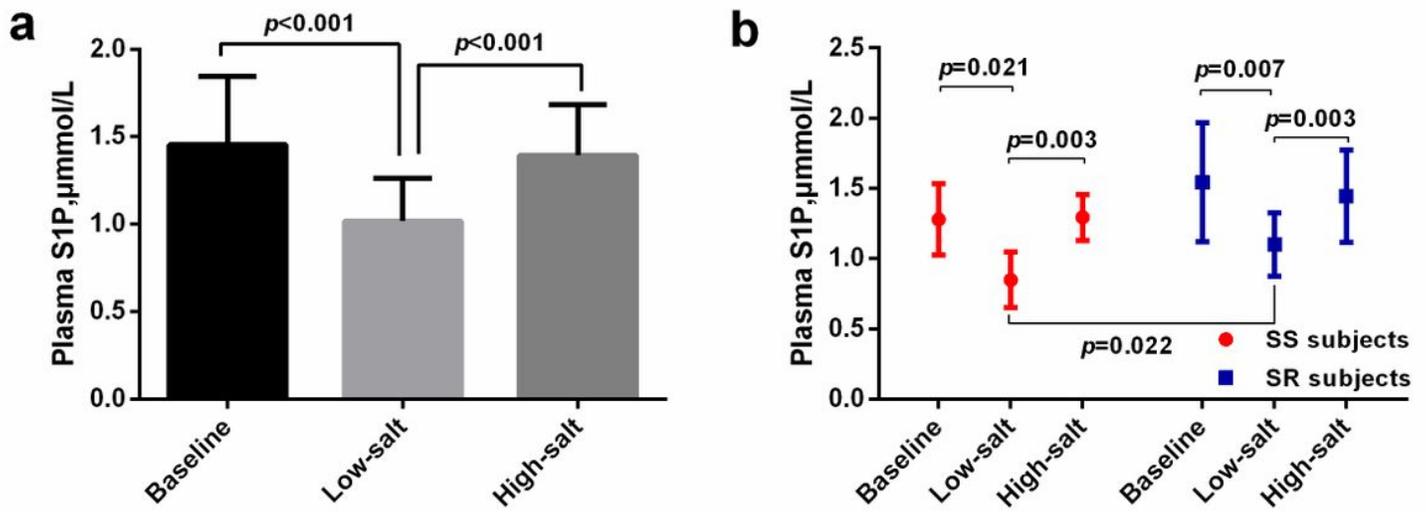


Figure 2

Effects of salt intervention on plasma S1P levels in the whole group (a) and in SS and SR subjects (b). Abbreviations: S1P, Sphingosine-1-Phosphate;SS,salt-sensitive;SR,salt-resistant.

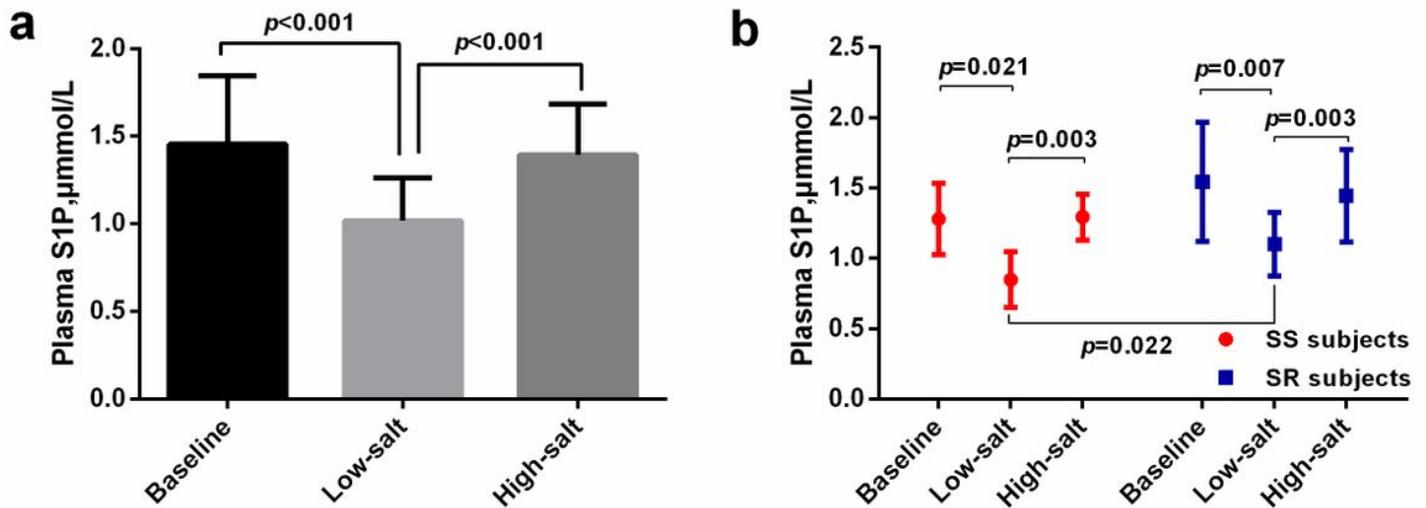


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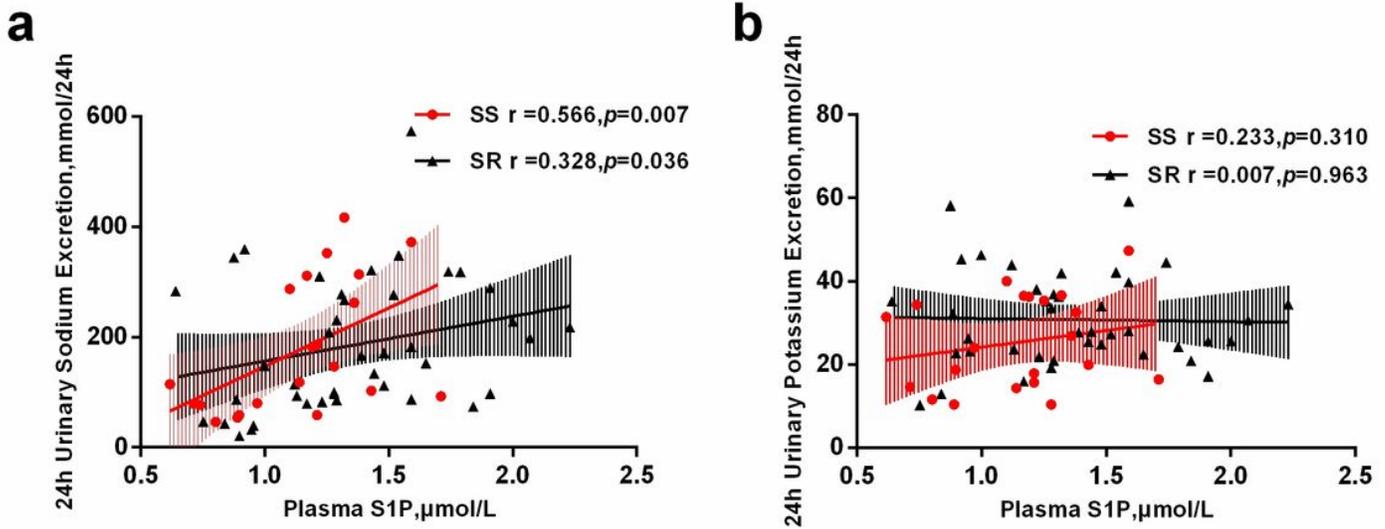


Figure 3

Correlations between S1P levels and 24-hour urinary sodium excretion (a) and potassium excretion (b) in SS and SR subjects. Abbreviations: S1P, Sphingosine-1-Phosphate; SS, salt-sensitive; SR, salt-resistant.

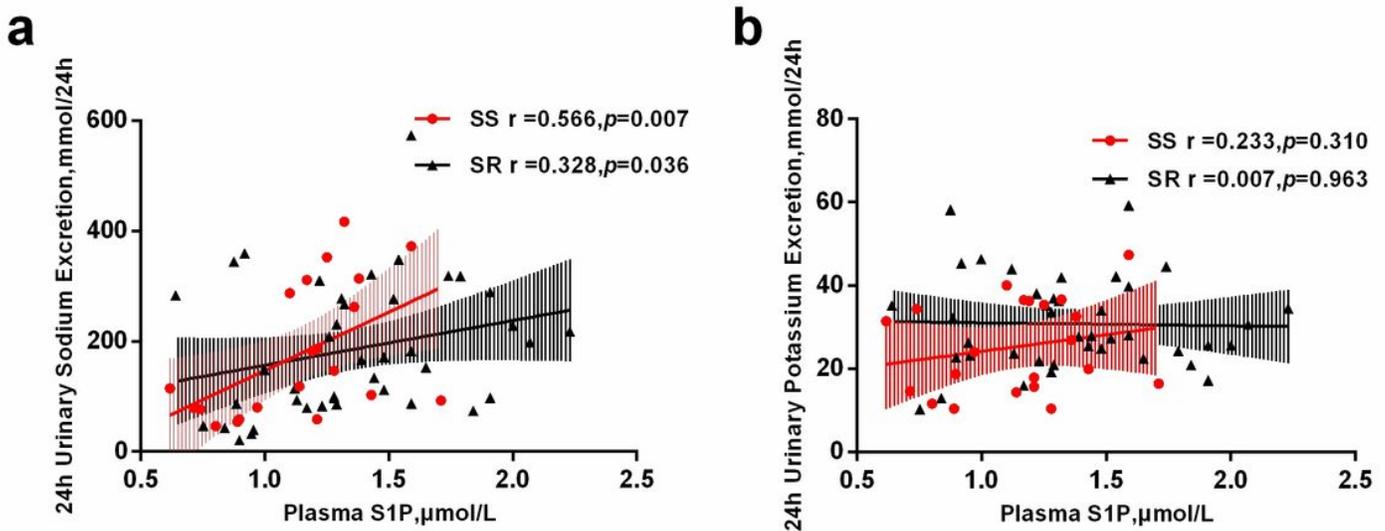


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Correlations between S1P levels and 24-hour urinary sodium excretion (a) and potassium excretion (b) in SS and SR subjects. Abbreviations: S1P, Sphingosine-1-Phosphate; SS, salt-sensitive; SR, salt-resistant.

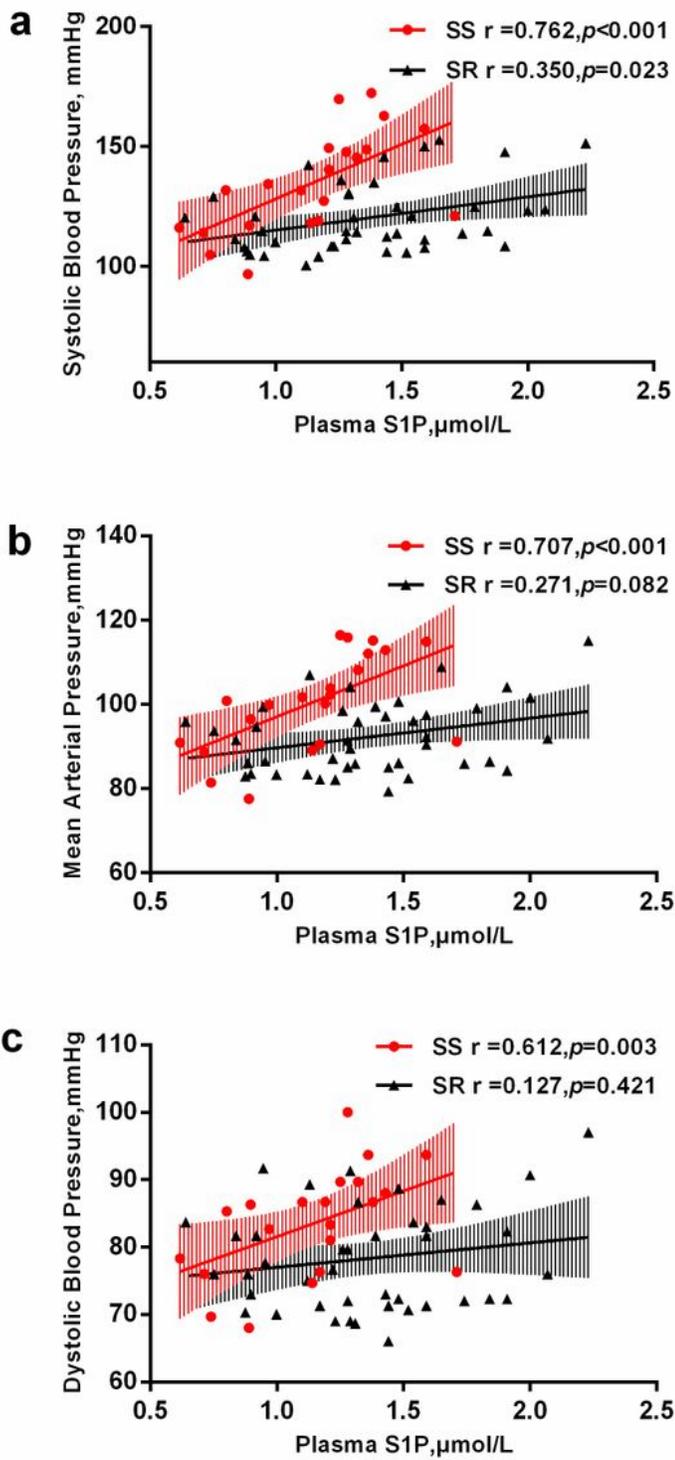


Figure 4

Correlations between S1P levels and systolic blood pressure (a), mean arterial pressure (b) and systolic blood pressure (c) in SS and SR subjects. Abbreviations: S1P, Sphingosine-1-Phosphate; SS, salt-sensitive; SR, salt-resistant.

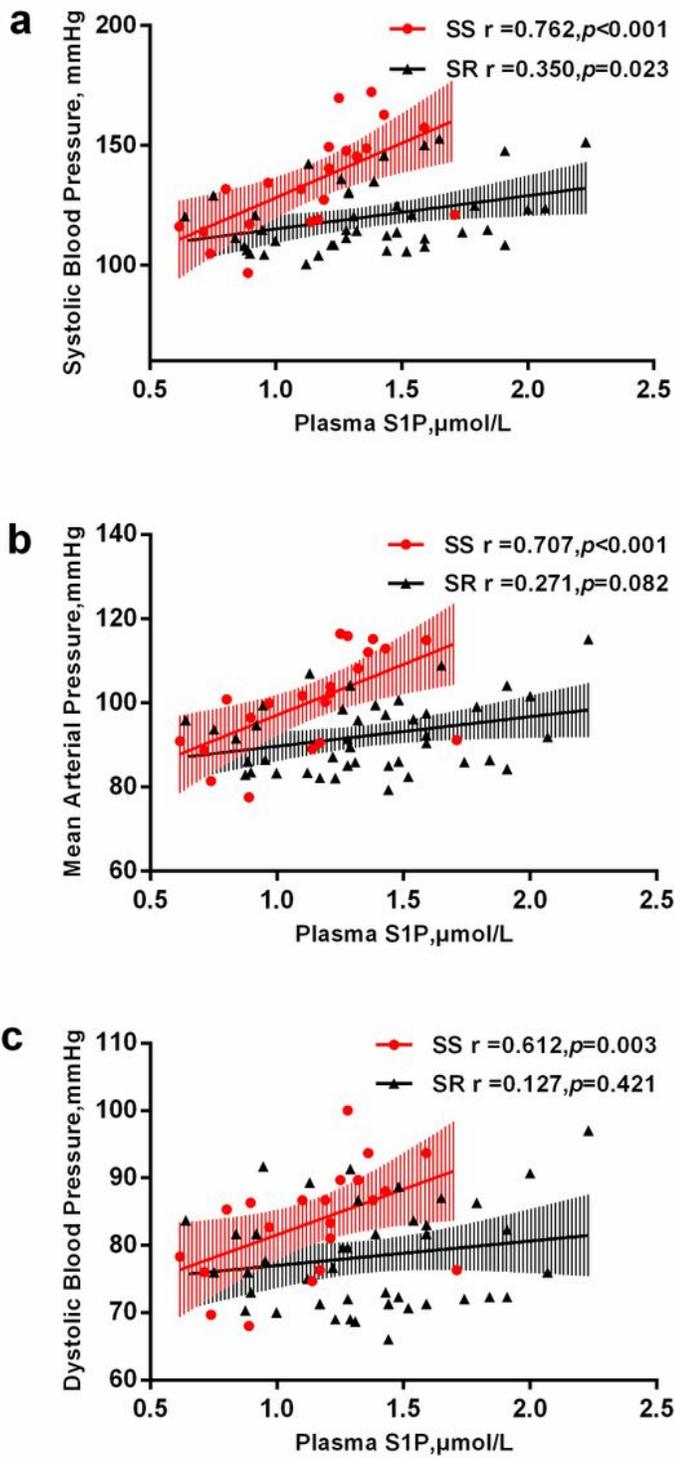


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