

## The association between S1P and vascular disease markers in the general population.

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**Funding Acknowledgements:** Type of funding sources: None.

### Introduction

Sphingosine-1-phosphate (S1P) is a lipid mediator of the immune system and vascular bed. However, cross-sectional analyses of S1P and parameters of vascular health in the population are sparse.

### Purpose

We explored the relation between S1P concentrations and several parameters of vascular health, i.e. ankle-brachial index (ABI), carotid intima-media thickness (cIMT), presence of carotid atherosclerotic plaques/stenosis, brachial artery flow-mediated dilation (FMD) as well as aortic wall thickness (AWT).

**Methods:** S1P was measured by liquid chromatography-tandem mass spectrometry in the population-based Study of Health in Pomerania (SHIP-TREND-0). ABI was calculated as the ratio of systolic blood pressure in arms and ankles. For cIMT, the distance between the lumen-intima and media-adventitia interfaces in longitudinal scans were measured. Carotid plaques were defined as a focal protrusion of the carotid vessel wall. Carotid stenosis was assessed with Doppler ultrasonography. FMD was evaluated by measuring the increase in brachial artery diameter after transient forearm ischemia. AWT was assessed by Magnetic Resonance Imaging. Subjects with cancer, severe renal insufficiency, previous myocardial infarction and extreme values for S1P (< 1st and > 99th percentile) were excluded. Sex stratified linear regression models adjusted for age, smoking, waist-to-hip ratio and platelets were used to assess the relation between S1P and vascular disease parameters.

**Results:** A total of n = 3,643 participants (48% male, median age 51, 25th and 75th percentile 39 and 63 years) could be included in the analyses. The median S1P concentration was 0.788  $\mu$ M (25th and 75th percentile 0.679 and 0.906, respectively). In men a 1 standard deviation higher S1P was associated with a significantly greater cIMT ( $\beta$ : 0.0057 95% confidence interval [CI]: 0.00027 to 0.0112 mm; p = 0.0396) and a lower ABI ( $\beta$ : -0.0090 (95% confidence interval [CI]: -0.0153 to -0.0029; p = 0.0038). In women S1P was significantly associated with cIMT ( $\beta$ : 0.0044 95% confidence interval [CI]: 0.0001 to 0.0086 mm; p = 0.0445) while no significant association was found for the relation of S1P with ABI. For both men and women S1P was not associated with FMD, the presence of carotid plaques/stenosis and AWT.

**Conclusions:** We found that S1P concentrations were positively related to a thicker cIMT in both sexes and lower ABI values in men. There was no association of S1P with any of the other vascular markers of interest. Future studies need to validate our results in other populations.