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# Association of suPAR with cardiovascular risk factors in a young and healthy population

Niklas Wohlwend<sup>a,b</sup>, Kirsten Grossmann<sup>b,c</sup>, Stefanie Aeschbacher<sup>d</sup>, Ornella C. Weideli<sup>b</sup>, Martin Risch<sup>b,e</sup>, Lorenz Risch<sup>b,c,f</sup>, David Conen<sup>e</sup>

<sup>a</sup> Faculty of Medicine, University of Bern, Bern, Switzerland; <sup>b</sup> Dr Risch Medical Laboratory, Vaduz, Liechtenstein; <sup>c</sup> Faculty of Medical Sciences, Private University in the Principality of Liechtenstein, Triesen, Liechtenstein; <sup>d</sup> Cardiovascular Research Institute Basel and Division of Cardiology, University Hospital Basel, University of Basel, Basel, Switzerland; <sup>e</sup> Division of Laboratory Medicine, Cantonal Hospital Graubünden, Chur, Switzerland; <sup>f</sup> Department of Laboratory Medicine, Institute of Clinical Chemistry, Inselspital Bern University Hospital, University of Berne, Berne, Switzerland; <sup>e</sup> Population Health Research Institute, McMaster University, Hamilton, Canada.



- Importance of biomarkers as predictors of individual cardiovascular risks
- Chronic low-grade inflammation is contributing to the development of cardiovascular diseases
- Soluble urokinase plasminogen activator receptor (suPAR) as correlate for lowgrade inflammation

Global burden of cardiovascular diseases

leading causes of disability adjusted life years (DALYs) and years of life lost (YLLs)

Prevalence of cardiovascular risk factors

## AIMS

- Primary objective:
- $\rightarrow$  Correlation of suPAR plasma levels with cardiovascular risk factors?
- Secondary objective:
- $\rightarrow$  Correlation of suPAR plasma levels with the healthy lifestyle score and the Framingham score?

### MATERIALS AND METHODS

#### Study population:

• Young and healthy adults (n= 2036) from the GAPP (Genetic and phenotypic determinants of blood pressure and other cardiovascular risk factors) study

#### Investigated parameters:

- Dependent variable: Soluble urokinase plasminogen activator receptor (suPAR)
- Independent variables: BMI, physical activity, alcohol consumption, smoking status, blood pressure parameters (office and ambulatory), glucose status, lipid levels, healthy lifestyle score\* and Framingham score\*\*

#### Statistical analyses:

- Baseline characteristics and analyses were done separately for male and female participants
- Comparison of independent variables amongst sex-specific suPAR plasma levels with ANOVA-analysis
- Sex-specific multivariable linear regressions of dependent variable with all independent variables separately adjusted for following potential confounders: office systolic blood pressure, age, BMI, physical, HbA1c, GFR, LDL,

Original **GAPP-Study population** (n = 2170; m = 1012, f = 1158)

Current main study population (n = 2036; m = 929, f = 1107)

HDL, smoking status, high sensitivity c-reactive protein.

\*Healthy lifestyle score: Ranging from 0-7; 1 point for each health metric fulfilled (including: BMI, blood pressure, LDL levels, HbA1c, smoking status, nutrition, extent of physical activity)

\*\*Framingham score: Ranging from 0-36 points for male and 0-38 points for female participants; estimate of 10-year risk of cardiovascular incident (including: age, blood pressure, HDL, total cholesterol, HbA1c/glucose levels, smoking status)

**Subpopulation** for analysis including parameters of ambulatory blood pressure (n = 1951; m = 897, f = 1054)

Figure 1: Study population flow chart

<b>ESULTS</b> Baseline characteristics:	Correlating cardiovascular risk factors and cardiovascular risk scores				Correlating cardiovascular risk factors and cardiovascular risk scores			
Sex-ratio: 46% male and 54% female participants	Male		Female		Male		Female	
Mean age in male and female study population: 37 years (31 – 40)	Variable	p-value	Variable	p-value	Variable	standardized β- coefficient (p-value)	Variable	standardized β- coefficient (p-value)
	HDL	<0.001	HDL	<0.001	HDL	-0.155 (<0.001)	HDL	- 0.114 (<0.001)
suPAR is lower in male (1.50 ng/ml $\pm$ 0.61) than in female (1.73 ng/ml $\pm$ 0.98; p-value < 0.001) participants	Current smoking	<0.001	Current smoking	<0.001	Current smoking	0.267 (0.001)	Current smoking	0.076 (0.017)
	Healthy lifestyle score	<0.001	HbA1c	<0.001	Healthy lifestyle score	-0.129 (0.001)	HbA1c	0.081 (0.008)
Higher prevalence of cardiovascular risk factors in male	Framingham Score	<0.001	Cholesterol	0.001	Framingham Score	0.161 (<0.001)	Cholesterol	-0.094 (0.001)

compared to female participants

 
 Table 1: Comparison of sex-specific quartiles of suPAR plasma level

 Table 2: Multivariable linear regression analyses
with one-way ANOVA

#### CONCLUSION

- suPAR plasma levels are strongly associated with cardiovascular risk factors, however sex-specific differences were found
- These sex-specific differences might be explained by the higher prevalence of cardiovascular risk factors in male participants and a comparatively young study population  $\rightarrow$  possible age-specific correlation of suPAR plasma levels and cardiovascular risk in female study population
- Laboratory testing in GAPP follow-up visits should again incorporate plasma suPAR levels to evaluate potential longitudinal age-specific differences  $\bullet$

- Frary CE, Biering-Sørensen T, Nochioka K, et al. Sex- and age-related differences in the predictive capability of circulating biomarkers: from the MONICA 10 cohort. Scand Cardiovasc J. 2021;55(2):65-72. doi:10.1080/14017431.2020.1853
- 5. Eugen-Olsen J, Andersen O, Linneberg A, et al. Circulating soluble urokinase plasminogen activator receptor predicts cancer, cardiovascular disease, diabetes and mortality in the general population. J Intern Med. 2010;268(3):296-308. doi:10.1111/j.1365-2796.2010.02252
- 6. Lyngbæk S, Marott JL, Sehestedt T, et al. Cardiovascular risk prediction in the general population with use of suPAR, CRP, and Framingham Risk Score. Int J Cardiol. 2013;167(6):2904-2911. doi:10.1016/j.ijcard.2012.07.018
- Persson M, Engström G, Björkbacka H, Hedblad B. Soluble urokinase plasminogen activator receptor in plasma is associated with incidence of CVD. Results from the Malmö Diet and Cancer Study. Atherosclerosis. 2012;220(2):502-505. doi:10.1016/j.atherosclerosis.2011.10.039
- Diederichsen MZ, Diederichsen SZ, Mickley H, et al. Prognostic value of suPAR and hs-CRP on cardiovascular disease. Atherosclerosis. 2018;271:245-251. doi:10.1016/j.atherosclerosis.2018.01.029

<sup>1.</sup> Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries, 1980-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet (London, England). 2018;392(10159):1736-1788. doi:10.1016/S0140-6736(18)32203-7

<sup>2.</sup> Pearson TA, Mensah GA, Alexander RW, et al. Markers of inflammation and cardiovascular disease: application to clinical and public healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. Circulation. 2003;107(3):499-511. doi:10.1161/01.cir.0000052939.59093.45

Conen D, Schön T, Aeschbacher S, et al. Genetic and phenotypic determinants of blood pressure and other cardiovascular risk factors: Methodology of a prospective, population-based cohort study. Swiss Med Wkly. 2013;143(January):1-9. doi:10.4414/smw.2013.13728