Decreased Arterial Vascular Tone in Small Arteries in Severe Hidradenitis Suppurativa – A Study Using Finger Photopulseplethysmography

A previous study has found an association between chronic inflammatory disorders e.g. psoriasis, rheumatoid arthritis, and inflammatory bowel disease and increased vascular stiffness(1). Psoriasis and hidradenitis suppurativa (HS) are believed to have shared comorbidities and pathophysiology despite their morphologically different manifestations in the skin.

In order to evaluate a putative association between the chronic inflammatory skin disease HS and arterial stiffness, an observational cross-sectional retrospective study was carried out as part of the Danish General Suburban Population Study (GESUS) (1), in which 430 patients with HS from the general population (representing mild HS; Table 1), 32 patients with HS from a hospital-based out-patient clinic (repre-

Table 1. Background factors and raw data ((# Missing values i.e. pulse trace data was not available in the data set on these study participants e.g. for outcome RI: 310/430= 72% missing values of the population HS group, 10/32=31% missing values of the Outpatient HS-group, and 16,029/20,780=77% missing values of the controls)

	Population HS-group n=430	**Out-patient clinic HS-group n=32**	**Controls n=20,780**
Age ((years) mean (range))	48 (22-78)	42 (22-64)	56 (20-96)
Sex % (number) Female vs. Male	68% vs. 32%	78% vs. 22%	54% vs. 46%
Smoking Status % (number) Present smoker Past smoker Never smoked	 41% 36% 23%	 55% 42% 3%	 18% 40% 42%
Ethnicity % (number) Caucasian	97%	97%	99%
CRP (median(mg/l)(range))	2.2 (0.1-38.0)	5.1 (0.2-119.0)	1.3 (0.1-194.0)
HS Severity Distribution Mild Moderate Severe Sartorius Score (median (range)) [lower quartile, upper quartile] Number of boils (median (range)) [lower quartile, upper quartile]	 50% 28.5% 21.5% Not Applicable Not Applicable 3 (2-106) [3-12.5]	 12.5% 15.5% 72% 29 (5-176) [25-50] 12 (1-171) [11-30]	 Not Applicable Not Applicable Not Applicable Not Applicable Not Applicable Not Applicable Not Applicable
Metabolic Syndrome	25%	53%	16%
Reflection Index (RI) (%) Mean (min-max)	 59.58 (19-88) (#310)	 46.09 (13-74) (#10)	 63.96 (5-96) (#16,029)
Stiffness Index (SI) (m/second) Mean (min-max)	 7.94 (5.11-13.62) (#310)	 7.02 (5.06-10.11) (#9)	 8.35 (1.22-21) (#16,010)
Vascular Age (VA) (years) Mean (min-max)	 38.67 (18-75) (#312)	 30.83 (18-59) (#9)	 41.65 (5-75) (#16,265)

senting severe HS, Table 1), and 20,780 controls underwent measurements of arterial vascular tone and stiffness using photoplethysmography (Pulse Trace PCA2®; Micro Medical Ltd, Kent, UK). The method of Pulse Trace has been validated by correlation with intra-arterial sensing techniques, and is a simple cost-effective screening method[2]. All analyses were performed using SAS 9.3.

This study was accepted by the ethics committee of Region Zealand (project number SJ-191, SJ-113, SJ-114) in Denmark (2,3).

RESULTS

Reflection index (RI) is an expression of arterial vascular tone and stiffness of small arteries. The raw data showed a significantly lower RI for both HS groups groups, compared to controls. The results remained significant when adjusting for confounders (age, sex, smoking and metabolic syndrome) in the out-patient clinic HS group (-11.26 (-17.75- -4.76), *P*=0.0002*), but not in the population HS group (Table 2).

Stiffness index (SI) expresses arterial stiffness in large arteries. Both HS groups showed no significant difference in either SI or vascular age in multivariate analysis, when compared with controls (Table 2).

DISCUSSION

This study suggests that decreased vascular tone and stiffness of small arteries may be associated with

Table 2. Unadjusted and adjusted Mean Difference (MD)

		Outpatient clinic HS-group Vs. Controls	Population HS-group Vs. Controls
Stiffness index (SI)			
I.	Unadjusted MD (95% CI)	**-1.33 (-2.41;-0.25) *P*=0.0120***	-0.42 (-0.90;0.06) *P*=0.0991
II.	Age-sex adjusted MD (95% CI)	0.01 (-0.92;0.94) *P*=0.9992	0.19 (-0.20;0.60) *P*=0.5053
III.	Age-sex-smoking adjusted MD (95%CI)	-0.20 (-1.15;0.76) *P*=0.8751	0.07 (-0.35;0.48) *P*=0.9224
IV.	Age-sex-smoking-diabetes adjusted MD (95%CI)	-0.20 (-1.15;0.76) *P*=0.8751	0.07 (-0.35;0.48) *P*=0.9224
V.	Age-sex-smoking-Hypertension adjusted MD (95%CI)	-0.27 (-1.21-0.68) *P*=0.7766	0.06 (-0.35-0.47) *P*=0.9367
VI.	Age-sex-smoking-MetS adjusted MD (95%CI)	-0.32 (-1.28-0.62) *P*=0.6883	0.06 (-0.04-0.50) *P*=0.9431
Reflection Index (RI)			
I.	Unadjusted MD (95% CI)	**-17.87 (-24.77;-10.96) *P*<.0001***	**-4.37 (-7.36;-1.38) *P*=0.0021***
II.	Age-sex adjusted MD (95% CI)	**-13.75 (-19.97;-7.17)** *P*<.0001*	-2.62 (-5.39;0.15) *P*=0.0673
III.	Age-sex-smoking adjusted MD (95%CI)	**-12.22 (-18.77;-5.66)** *P*<.0001*	-2.73 (-5.52;0.06) *P*=0.0560
IV.	Age-sex-smoking-diabetes adjusted MD (95%CI)	**-12.22 (-18.77;-5.66)** *P*<.0001*	-2.73 (-5.52;0.06) *P*=0.05606
V.	Age-sex-smoking-Hypertension adjusted MD (95%CI)	**-12.02 (-18.57- -5.47)** *P*<.0001	-2.70 (-5.49- -0.08) *P*=0.0586
VI.	Age-sex-smoking-MetS adjusted MD (95%CI)	**-11.26 (-17.75- -4.76)** *P*=0.0002*	-1.74 (-4.68-1.20) *P*=0.3356
Vascular Age (VA)			
I.	Unadjusted MD (95% CI)	**-10.83 (-19.50;-2.15) *P*=0.0105***	-2.98 (-6.85;-0.89) *P*=0.1621
II.	Age-sex adjusted MD (95% CI)	-0.35 (-7.89;-7.18) *P*=0.9931	1.74 (-1.62;5.10) *P*=0.4328
III.	Age-sex-smoking adjusted MD (95%CI)	-2.09 (-9.81;5.63) *P*=0.7927	0.66 (-2.73;4.04) *P*=0.8879
IV.	Age-sex-smoking-diabetes adjusted MD (95%CI)	-2.09 (-9.81;5.63) *P*=0.7927	0.66 (-2.73-4.04) *P*=0.8879
V.	Age-sex-smoking-Hypertension adjusted MD (95%CI)	-2.62 (-10.29-5.04) *P*=0.6908	0.63 (-2.73-4.00) *P*=0.8933
VI.	Age-sex-smoking-MetS adjusted MD (95%CI)	-3.19 (-10.86-4.48) *P*=0.5799	0.52 (-3.07-4.11) *P*=0.9352

95% CI: 95% confidence interval; *statistically significant at a 0.05 level

severe HS, and at the same time found no difference in arterial stiffness in large arteries. The significance for the out-patient clinic HS group, but not the population HS group may reflect a dose-response relationship.

Vascular tone in vascular smooth muscle cells of small arteries depends on competing vasodilators and vasoconstrictors. We speculate that the inflammation of HS may induce a dysfunctional balance e.g. through increased TNF-alpha with subsequent increase of the vasodilator nitric oxide resulting in the lower arterial vascular tone observed. Additionally, mast cells are increased in HS [4], possibly increasing levels of the vasodilator histamine. HS patients often suffer from stress which could increase sympathetic activity, thereby adrenalin/cortisol and subsequent vasodilation in e.g. muscles.

The more peripheral an artery is, the more collagen it contains and the stiffer it is. The finding of lower vascular tone may also be suggestive of a different elastin:collagen ratio in small arteries in HS. The healing process of HS lesions is known to involve scarring formation of sinus tracts [5], which may suggest a hypothesis of altered connective tissue.

This study found no difference in SI expressing arterial stiffness of large arteries between HS and controls. Our previous study found an association between HS and myocardial infarction, but no association with stroke, nor peripheral arterial stiffness of lower extremities in medium/large arteries [6], suggesting regional differences in vascular beds in HS.

The major limitation of the study is the missing values of pulse trace measurement (Table 1) creating possible selection bias.

Although unable to draw any clinical conclusions, we believe these results may contribute to the future research of the complexity of HS and cardiovascular risk profiling.

This study suggests that decreased vascular tone and stiffness of small arteries may be associated with severe HS, and at the same time found no difference in arterial stiffness in large arteries. The significance for the out-patient clinic HS group, but not the population HS group may reflect a dose-response relationship.

Vascular tone in vascular smooth muscle cells of small arteries depends on competing vasodilators and vasoconstrictors. We speculate that the inflammation of HS may induce a dysfunctional balance e.g. through increased TNF-alpha with subsequent increase of the vasodilator nitric oxide resulting in the lower arterial vascular tone observed. Additionally, mast cells are increased in HS [4], possibly increasing levels of the vasodilator histamine. HS patients often suffer from stress which could increase sympathetic activity, thereby adrenalin/cortisol and subsequent vasodilation in e.g. muscles.

The more peripheral an artery is, the more collagen it contains and the stiffer it is. The finding of lower vascular tone may also be suggestive of a different elastin:collagen ratio in small arteries in HS. The healing process of HS lesions is known to involve scarring formation of sinus tracts [5], which may suggest a hypothesis of altered connective tissue.

This study found no difference in SI expressing arterial stiffness of large arteries between HS and controls. Our previous study found an association between HS and myocardial infarction, but no association with stroke, nor peripheral arterial stiffness of lower extremities in medium/large arteries [6], suggesting regional differences in vascular beds in HS.

The major limitation of the study is the missing values of pulse trace measurement (Table 1) creating possible selection bias.

Although unable to draw any clinical conclusions, we believe these results may contribute to the future research of the complexity of HS and cardiovascular risk profiling.

References:

1. Dregan A. Arterial stiffness association with chronic inflammatory disorders in the UK Biobank study. Heart Br Card Soc. 2018;104:1257-62.
2. Bergholdt HKM, Bathum L, Kvetny J, Rasmussen DB, Moldow B, Hoeg T, et al. Study design, participation and characteristics of the Danish General Suburban Population Study. Dan Med J 2013 Sep;60:A4693.
3. Salvi P, Magnani E, Valbusa F, Agnoletti D, Alecu C, Joly L, Benetos A. Comparative study of methodologies for pulse wave velocity estimation. J Hum Hypertens. 2008 Oct;22:669-77.
4. List EK, Pascual JC, Zarchi K, Nürnberg BM, Jemec GBE. Mast cells in hidradenitis suppurativa: a clinicopathological study. Arch Dermatol Res. 2019;311:331-5.
5. Jemec GBE. (2012) Clinical practice. Hidradenitis suppurativa. N Engl J Med. 2012;366:158-64.
6. Miller IM, Ahlehoff O, Zarchi K, Rytgaard H, Mogensen UB, Ellervik C, et al. Hidradenitis suppurativa is associated with myocardial infarction, but not stroke or peripheral arterial disease of the lower extremities. Br J Dermatol. 2018 Mar;178:790-791.

Acta Dermatovenerol Croat
2022;30(2):119-122

Iben Marie Miller[1], Ole Ahlehoff[2], Kian Zarchi[3], Helene Rytgaard[4], Ulla B. Mogensen[4], Christina Ellervik[5], Gregor B. E. Jemec[6]

[1]Department of Dermatology, Zealand University Hospital (Roskilde), Roskilde, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

[2]Department of Cardiology, The Heart Centre, Rigshospitalet, Blegdamsvej, Denmark

[3]Department of Dermatology, Roskilde Hospital, Roskilde, Denmark

[4]Department of Biostatistics, University of Copenhagen, Copenhagen, Denmark

[5]Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark and Department of Research, Nykøbing Falster Hospital, Nykøbing Falster, Denmark

[6]Department of Dermatology, Roskilde Hospital, Roskilde, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

Corresponding author:

Iben Marie Miller, MD, PhD

Department of Dermatology, Zealand University Hospital

Sygehusvej 10, 4000 Roskilde,

Faculty of Health and Medical Sciences, University of Copenhagen, Denmark

ibenmariemiller@gmail.com

Received: January 19, 2022

Accepted: March 1, 2022

Conflict of interest/Funding:

None with the subject matter discussed in this manuscript.

The Study was funded by the Region Zealand Foundation.

The results presented in this paper have not been previously published or presented orally in whole or in part.