Epidemiology and determinants of facial telangiectasia: a cross-sectional study

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ABSTRACT

Background: Telangiectasia or red veins are one of the prominent features of facial skin aging. To date, there are few studies investigating the determinants of telangiectasia.

Objectives: We investigated lifestyle and physiological factors associated with facial telangiectasia in a large prospective Dutch cohort study.

Methods: Telangiectasia were quantified digitally from standardized facial photographs of 2842 northwestern European participants (56.8% female, median age 66.9) from the Rotterdam Study, collected in 2010-2013. Effect estimates from multivariable linear regressions are presented as the percentage difference in the mean value of telangiectasia area per unit increase of a determinant (%Δ) with corresponding 95% CI.

Results: Significant determinants were older age (1.7%Δ per year, 95%CI 1.4 to 2.0), female sex (18.3%Δ, 95%CI 13.2 to 23.6), smoking (current versus never 38.4%Δ, 95%CI 30.3 to 47.0; former versus never 11.6%Δ, 95%CI 6.6 to 16.9), a high susceptibility to sunburn (10.2%Δ, 95%CI 5.4 to 15.3), and light skin color (pale versus white-to-olive 31.4%Δ, 95%CI 19.7 to 44.1; white vs. white-to-olive 9.2%Δ, 95%CI 2.8 to 16.0).

Conclusions: In this large cohort study, we confirmed known and described new determinants of facial telangiectasia.

INTRODUCTION

Facial telangiectasia are a feature of skin aging, alongside wrinkling, pigmented spots, and sagging. Most skin aging studies have focused on aging as a compound phenotype, predominantly using manual photonumeric scales[1-3]. This makes it difficult to make inference on the role of lifestyle and physiological factors associated with specific features such as telangiectasia, if they have varying influence on different skin aging features.

In line with this, recent skin aging research into pigmented spots, wrinkles, and sagging eyelids showed differences in genetic background as well as different environmental risk factors per subtype[4-6]. This highlights the need for separate analysis of risk factors for telangiectasia.

To date, few studies have specifically focused on telangiectasia. In one cross-sectional study of 1400 subjects (aged 20-54 years), telangiectasia were associated with increasing age, male sex, fair skin, smoking, and mainly outdoor occupations[7]. Smoking has repeatedly been associated with telangiectasia[8,9], but little is known about other lifestyle and physiological factors associated with red veins in the middle-aged to elderly.

In the Rotterdam Study, a large population-based cohort study, we investigated multiple lifestyle and physiological factors associated with facial telangiectasia in 2842 northwestern European elderly, using multiple linear regression.

METHODS

Study design, setting and participants

The Rotterdam Study (RS) is an ongoing prospective population-based cohort study of middle-aged to elderly (≥45 years of age) inhabitants of Ommoord, a suburb of Rotterdam in the Netherlands[10]. Since 2010, skin examinations have been conducted by trained physicians, focusing on the most common skin diseases. In addition, standardized high-resolution digital facial photographs (Premier 3dMDface3-plus UHD, Atlanta, GA, USA) are collected of participants not wearing make-up, cream, or jewelry. The present study aimed to include all participants who visited the dermatological screening at the research center between September 2010 and July 2013. For this study, a cross-sectional design was applied where data were measured at a single moment. The Rotterdam Study has been approved by the institutional review board (Medical Ethics Committee) of the Erasmus University Medical Center and by the review board of The Netherlands Ministry of Health, Welfare and Sports[10]. All participants provided written informed consent to participate in the study.

Telangiectasia assessment

The presence of telangiectasia was digitally quantified using semi-automated image analysis of high-resolution facial frontal photographs. The algorithms, digital rendering, measurement,

and validation with numerical grading have been described in detail previously[11]. In short, the analysis detects areas that are colored red to purple and linear or branch-like in shape (Figure 1). It subsequently calculates the percentage of skin area detected as telangiectasia.
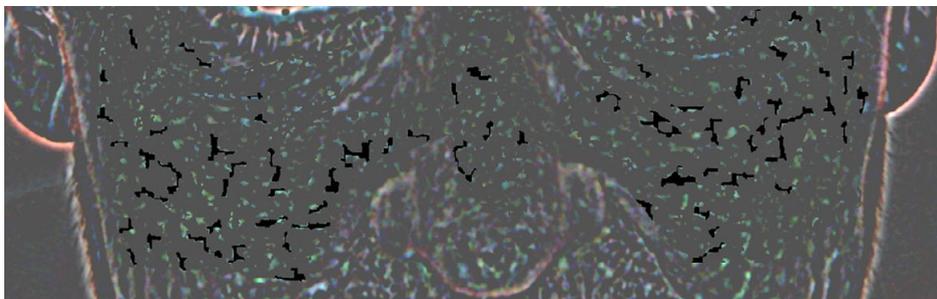
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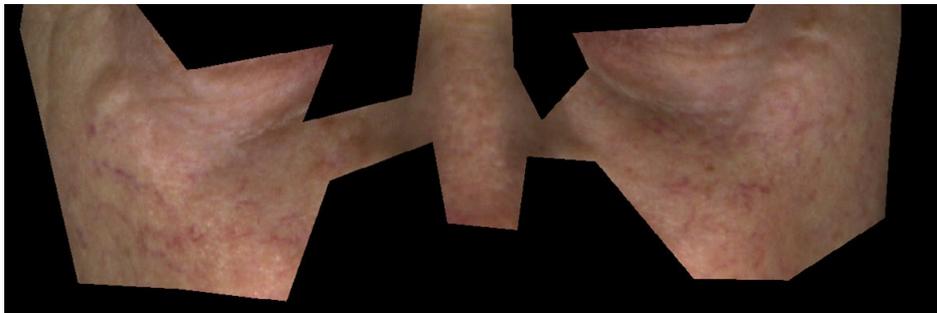
B

Figure 1. (**A**) Example of masked image. (**B**) Example of image analysis technique; the black structures are picked up as telangiectasia.

Determinants

Variables were selected based on known literature and biologically plausible associations. Level of education, smoking habit, alcohol consumption, and UV-related questions were collected through interview[12]. Variables collected by physical examination were body mass index (BMI), presence of dry skin, validated constitutional skin color assessment at sun-protected sites (pale, white, and white-to-olive)[13], rosacea (graded as centrofacial redness and red papules), and baldness. We used the Norwood-Hamilton scale[14,15] for baldness in men and the Ludwig scale[16] for baldness in women and classified these into none to minimal, moderate, and extensive baldness. Serum estradiol, testosterone and sex hormone binding globulin (SHBG) were measured on average 5.6 years before photograph collection. For women, the free androgen index (FAI) was calculated: (total testosterone / SHBG $*$ 100)[17]. Details of all variables have been previously published[4].

Statistical analysis

We excluded variables with >35% missing values, namely the UV variables "outdoor work history" and "frequency of tanning bed visits". For the other missing values (maximum per variable: 16.4%), we performed multiple imputation based on all available variables shown in Table 1, with 20 iterations. To investigate the associations between lifestyle and physiological factors and telangiectasia, we used multivariable linear regressions, where all these variables are adjusted for one another in one model. Additionally, we adjusted for two technical variables in all analyses: one which accounted for possible variations in resolutions and another which accounted for variation in flash light[11,13]. Interaction terms for age, sex, smoking, and UV variables were tested. They were not significant or did not change the betas significantly and hence not added to our model.

Because the residuals of the linear regression of telangiectasia area did not fit a normal distribution, we transformed the outcome using the natural logarithm (ln), resulting in an approximately normal distribution of the regression residuals. To interpret the effect estimates (regression betas), we transformed the betas back, using the formula: $(exp^{\beta}-1) * 100\%$. This outcome is interpreted as the percentage change (%Δ): the percentage increase in the mean value of telangiectasia area per unit increase of the independent variable, e.g. 3% increase in telangiectasia area per 1 year of age. There was no statistical interaction between sex and other variables (data not shown); therefore, all analyses were performed for men and women together. FAI, estradiol, and testosterone, hence, were excluded from this analysis. All analyses were performed using SPSS for Windows version 21.0 (SPSS, Chicago, IL) and software package R. A two-sided P-value of <0.05 was considered statistically significant.

Sensitivity and additional analyses

The missing UV variables ("outdoor work history" and "tanning bed use"), which were missing for ≥35% of the participants, were analyzed for association with telangiectasia in an exploratory complete-case analysis. Rosacea could have falsely been detected as telangiectasia, although people with rosacea do not necessarily show telangiectasia. In the RS cohort, we manually graded 54 individuals as having rosacea. To show their relationship, we calculated the correlation coefficient between rosacea and telangiectasia area. Lastly, we also retrieved data on telangiectasia from another cohort, the German SALIA cohort of elderly women. Because this cohort was a lot smaller, contained only women, and was different in terms of telangiectasia assessment and studied determinants, information on methods and results of these analyses is presented separately in the Supplementary Material. In an attempt to make a comparison between the RS and the SALIA cohort, we performed a linear regression analysis in RS women only, also including the variables FAI and estradiol.

Table 1. Characteristics of 2842 participants of the Rotterdam Study with telangiectasia measurements

Characteristic	Men N=1321	Women N=1521
Telangiectasia % - median [IQR]	0.77 [0.49 – 1.21]	0.96 [0.62 – 1.41]
Age at photo in years - median [IQR]	66.80 [61.3 – 72.0]	66.39 [61.0 – 71.3]
BMI in kg/m^2 - mean (SD)	27.70 (3.70)	27.56 (4.76)
Skin color		
pale (%)	100 (7.57)	141 (9.27)
white (%)	1014 (76.76)	1196 (78.63)
white-to-olive (%)	207 (15.67)	184 (12.10)
Baldness[a]		
no/mild baldness (%)	656 (49.66)	1013 (66.60)
moderate (%)	299 (22.63)	365 (24.00)
extensive (%)	365 (27.63)	111 (7.30)
Tendency to develop sunburn		
low (%)	870 (65.86)	921 (60.55)
high (%)	414 (31.34)	528 (34.71)
Outdoor work history		
no (%)	536 (40.58)	717 (47.14)
yes (%)	244 (18.47)	140 (9.20)
missing (%)	541 (40.95)	664 (43.66)
History of living in a sunny country >1 year		
no (%)	1178 (89.17)	1399 (91.98)
yes (%)	118 (8.93)	67 (4.40)
Sun-protective behavior[b]		
never/almost never (%)	482 (36.49)	485 (31.89)
often/almost always/always (%)	814 (61.62)	980 (64.43)
Tanning bed use		
never or less than 10x (%)	631 (47.77)	717 (47.14)
more than 10x (%)	74 (5.60)	140 (9.20)
missing (%)	616 (46.63)	664 (43.66)
Spend winter in sunny country		
no or less than 1 month (%)	1169 (88.49)	1366 (89.81)
yes, ≥1 month/yr (%)	61 (4.62)	69 (4.54)
missing (%)	91 (6.89)	86 (5.52)
Smoking history[c]		
current (%)	275 (19.45)	241 (15.84)
former (%)	766 (57.99)	695 (45.69)
never (%)	280 (21.20)	583 (38.33)
Education level[d]		
low (%)	91 (6.89)	139 (9.14)
medium (%)	745 (56.40)	1021 (67.13)
high (%)	469 (35.50)	349 (22.95)

Table 1. Characteristics of 2842 participants of the Rotterdam Study with telangiectasia measurements (continued)

Characteristic	Men N=1321	Women N=1521
Alcohol		
median use in glasses/day [IQR]	1.24 [0.31 – 2.42]	0.45 [0.05 – 1.40]
missing (%)	242 (18.32)	225 (14.79)
Dry skin		
No (%)	444 (33.61)	388 (25.51)
Yes (%)	877 (66.39)	1132 (74.42)
Testosterone in nmol/l - median [IQR]	16.58 [13.09 – 20.48]	na
Free androgen index[e] - median [IQR]	na	1.34 [0.89 – 1.93]
missing (%)		76 (5.00)
Estradiol in pmol/l - median [IQR]	na	39.72 [18.35 – 73.09]

Abbreviatons: BMI, body mass index; IQR, interquartile range; na, not applicable; SD, standard deviation.
[a]based on the Norwood-Hamilton (NH) scale for men and the Ludwig scale for women; None or minimal: NH score 1, 2, 3, 9, 10, 11 and Ludwig scale score none. Moderate: NH score 4, 5, 6, 12 and Ludwig scale score 1. Extensive: NH score 7, 8 and Ludwig scale score 2, 3; [b]wearing sunglasses and/or a brimmed hat in the sunshine; [c]cigars, cigarettes or pipe; [d]low (primary education); medium (lower secondary education/lower vocational education/intermediate vocational education); high (general secondary education/higher vocational education/university); [e]free androgen index (calculated as total testosterone in nmol/l divided by sex hormone binding globulin in nmol/l).

RESULTS

Study population

Between September 2010 and July 2013, a total of 3831 participants visited the dermatological examination of the RS. We excluded individuals due to non-northwestern European origin, poor image quality, and make-up, leaving 2842 participants with eligible 3D photographs used to measure facial telangiectasia area. There were slightly more women than men (N=1521; 53.5%), and the median age was 66.6 years old (Table 1). The median telangiectasia area was higher in women than in men (men: 0.77%, IQR 0.49 to 1.21; women: 0.96%, IQR 0.62 to 1.41).

Determinants for facial telangiectasia area

With higher age, telangiectasia area increased 1.7% per year (95%CI 1.4 to 2.0). Women had 18.3% (95%CI 13.2 to 23.6) more telangiectasia than men, and the lighter the skin color, the higher the risk for more red veins was. Having a white skin color associated with a 9.2% (95%CI 2.8 to 16.0) larger telangiectasia area and having a pale skin color with 31.4% more red veins, compared to white-to-olive skinned participants. Interestingly, not only did current smokers have 38.4% (95%CI 30.3 to 47.0) more telangiectasia than non-smokers, but former smokers also had 11.6% (95%CI 6.6 to 16.9) more telangiectasia than non-smokers. Finally, participants with a tendency to develop sunburn also showed a 10.2% (95%CI 5.4 to 15.3) larger telangiectasia area than those not susceptible to sunburn (Table 2).

Table 2. Multivariable linear regression of facial telangiectasia: determinants of facial telangiectasia among 2842 participants of the Rotterdam Study

Determinant	%Δ telangiectasia area[a]	95% CI	P-value
Sex			
male	ref	ref	ref
female	**18.3**	**[13.2 – 23.6]**	**<0.001**
Age (per year)	**1.7**	**[1.4 – 2.0]**	**<0.001**
BMI (per point)	0.2	[-0.2 – 0.7]	0.405
Skin color			
white-to- olive	ref	ref	ref
white	**9.2**	**[2.8 – 16.0]**	**0.004**
pale	**31.4**	**[19.7 – 44.1]**	**<0.001**
Baldness			
no/mild baldness	ref	ref	ref
moderate	1.7	[-3.1 – 6.8]	0.500
extensive	$-1.1*10^{-2}$	[-5.7 – 11.0]	0.997
Tendency to develop sunburn	**10.2**	**[5.4 – 15.3]**	**<0.001**
History of living in a sunny country	0.5	[-7.3 – 8.9]	0.905
Sun-protective behavior[b]	-0.6	[-4.8 – 3.7]	0.772
Spending winter in sunny country	-8.1	[-16.4 – 0.9]	0.076
Smoking history[c]			
never	ref	ref	ref
former	**11.6**	**[6.6 – 16.9]**	**<0.001**
current	**38.4**	**[30.3 – 47.0]**	**<0.001**
Education level[d]			
low	ref	ref	ref
medium	4.31	[-3.23 – 12.4]	0.270
high	2.26	[-5.76 – 11.0]	0.592
Alcohol (per glass per day)	-0.8	[-2.2 – 0.7]	0.291
Dry skin			
no	ref	ref	ref
yes	-1.5	[-5.8 – 3.1]	0.519
Batch[e]	**32.26**	**[23.4 – 41.7]**	**<0.001**
Residual[f]	**2.27**	**[2.0 – 2.5]**	**<0.001**

Abbreviations: 95% CI, 95% conference interval; BMI, body mass index; ref, reference variable. Boldface indicates statistically significant determinants.

[a] %Δ: the percentage change in telangiectasia area (the % increase in the mean value of telangiectasia area per unit increase of the independent variable, calculated by the formula: $(exp^{β}-1) \cdot 100\%$. E.g. 1.7% increase in telangiectasia area per 1 year of age; [b]wearing sunglasses and/or a brimmed hat in the sunshine; [c]cigars, cigarettes or pipe; [d]low (primary education); medium (lower secondary education/lower vocational education/intermediate vocational education); high (general secondary education/higher vocational education/university); [e]technical variable which accounts for possible changes in resolution; [f]technical variable which accounts for possible changes in flash light variability. R^2 total model: 0.354.

Sensitivity and additional analyses

In a complete case analysis including the two additional UV variables "outdoor work history" and "tanning bed use", both were not significantly associated (Supplementary Table S1). Additionally, the effect estimates of the significant determinants remained similar to the previous analysis, indicating there was no meaningful association between these two UV variables and telangiectasia. However, the variable "spending winter in a sunny country" showed a negative association (-20.8%, 95%CI -31.4 to -8.5) instead of no association in the previous analysis. Spearman's rho correlation coefficient between rosacea and telangiectasia area was 0.04, indicating no correlation between the two conditions. In the SALIA cohort, age, light skin color type, and smoking were significantly associated determinants (Supplementary Material & Supplementary Tables S3 and S4).

When analyzing RS women only (N=1521), we found similar results to those in the analysis of men and women together. The only meaningful difference was that BMI was associated with more telangiectasia area in women (0.6%Δ per 1 point BMI increase, 95%CI 0.1 to 1.2) (Supplementary Table S2).

DISCUSSION

In this large cross-sectional study, the most important variables associated with facial telangiectasia were light skin color type and smoking. Increasing age was also significantly associated with more facial red veins, although with a smaller effect size. Additionally, we found that female sex and tendency to develop sunburn were significant determinants for telangiectasia in the RS. We replicated our associations in a smaller cohort of women from European ancestry, showing the relevance of our findings. Although the cohort was smaller and only assessed telangiectasia in women with a different assessment, we demonstrated that main determinants were indeed associated with telangiectasia.

Smoking was the most important determinant for telangiectasia with the largest effect size. Current smokers had more than a third extra telangiectasia compared with non-smokers. This is not surprising, as we know that smoking is one of the most important lifestyle factors inducing premature skin aging[9,18-20]. It might even be the most important risk factor for telangiectasia since it is repeatedly replicated in all telangiectasia studies. Even former smoking had a significant effect in our cohort. The underlying mechanism on how smoking could lead to more red veins is not yet known; however, smoking induces DNA damage, elastosis, and more atrophy of the skin, which could make red veins more visible[21]. Smoking has also been associated with dilated venules in other human organs such as the retina[22]. Alternatively, smoking causes vasoconstriction of the small vessels which leads to a chronic hypoxemic state in the skin[23]. This could result in proliferation of new red veins, visible as more telangiectasia.

Pale skin color type was associated with more telangiectasia, as previously reported[7]. Similar to smoking, the underlying mechanism is not yet elucidated, but we hypothesize that UV-induced DNA damage will play a role, as in other types of skin aging. Alternatively, telangiectasia might be more visible on lighter skin.

Female sex was associated with more telangiectasia, which was opposite to what has been previously reported[7]. This could be explained in part by the higher average age in the RS population compared to the age of the participants in the previous report. Men tend to show signs of skin wrinkling earlier in life, with women showing similar wrinkling prevalence as men later on in life[4]. Hence, men could also develop telangiectasia earlier in life. Additionally, male skin is 10-20% thicker than female skin and therefore might be less susceptible to thinning and showing red veins[24].

Light skin color type and current smoking were also significant determinants for telangiectasia in the SALIA cohort. Unexpectedly, in this relatively small cohort, older age was associated with less telangiectasia. However, the age range of the replication cohort is much smaller than in the RS and lies within the ages in which the RS also showed a decline in telangiectasia (Supplementary Figures S1 and S2). This phenomenon has not been described earlier, which indicates it is probably a coincidental finding. However, unknown confounders might also have a part in this. In the sensitivity analysis in the women of the RS, we found that increasing BMI associates with more telangiectasia but this was not found in the SALIA cohort. A higher BMI has previously been linked with fewer facial wrinkles, which probably has to do with the filler effect of facial fat[4]. Research into skin circulation showed that with increasing BMI, oxygenation in skin increased[25]. Furthermore, dermal microvascular dysfunction is common in diabetes patients who often have a higher BMI than healthy subjects[26]. However, how BMI exactly associates with telangiectasia remains to be fully understood.

The results of this study confirm the hypothesis that the different features of skin aging have different determinants. Age and sun exposure are the exception and are important risk factors for all skin aging phenotypes (i.e., wrinkling, pigmented spots, and telangiectasia). However, skin color, for example, is different. Pale skinned individuals are more at risk for having telangiectasia and pigmented spots while they have less wrinkles[4,5]. Smoking is the major lifestyle risk factor for wrinkling and telangiectasia, and although it can cause smokers' melanosis in the oral cavity[27], it has not been proven to stimulate facial pigmented spots. This clustering of specific risk factors could be of use in the risk stratification and personalized approach of skin aging prevention strategies.

There are several limitations of this study. Firstly, the cross-sectional nature of the associations prevents from determining causal inferences. Secondly, we used a digital method to measure telangiectasia where most previously performed studies used photonumeric grading. However, validation of our digital method[11] has shown that there is a moderate to good correlation between digital and photonumeric measurement of telangiectasia (Spearman's rho 0.60 in women and 0.75 in men), which suggests this will not have a large effect in our conclusions. Also, we found

only one of our UV variables to be associated with telangiectasia. This illustrates that the quality of our used questions for sun exposure was suboptimal and that it remains a difficult variable to capture by questionnaire. Furthermore, besides in telangiectatic aging, facial erythema and telangiectasia are also often associated with the erythematotelangiectatic subtype of rosacea (ETR, besides the other three types of rosacea: papulopustular, phymatous and ocular). It is therefore important to recognize the differences between ETR and telangiectatic aging[28]. However, in our data, the number of rosacea patients was low and rosacea correlated poorly with telangiectasia. Looking more carefully into these rosacea cases, there was a substantial proportion with the papulopustular subtype and telangiectasia were poorly picked up in the ETR group. The latter is a limitation of our image analysis technique where it seems to pick up telangiectasia less well in an erythematous environment, probably due to lack of contrast. Lastly, our findings hold for a predominantly northwestern European population. It is not clear to which extent these can be extrapolated to other populations.

In conclusion, this large study confirmed some of the earlier found risk factors for telangiectasia such as pale skin and smoking which are similar in men and women, while identifying potential new associations such as BMI. These results support the evidence that different skin colors show varying prevalence of specific skin aging features. The correlated factors of telangiectasia can help future studies to unravel causal versus consequence determinants as more insight into etiology of telangiectasia is gained, and longitudinal or experimental studies are added to this field of research.

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SUPPLEMENTARY MATERIAL (SALIA COHORT)

METHODS

Study population

The Study on the influence of Air pollution on Lung function, Inflammation and Ageing (SALIA) is a cohort study including middle-aged women from the urban Ruhr area (Dortmund, Duisburg, Essen, Gelsenkirchen and Herne) and two rural northern counties (Southern Münsterland) in West Germany. The baseline investigation started in 1985, when the women were about 55 years of age. Men were not recruited because of the high occupational exposure of many men in this area, where coal mining and steel industry constituted the predominant sources of income in the time period before the baseline examination[1]. The replication analysis is based on data from the clinical follow-up examination (2007–2010), in which 834 women participated. All participants gave written informed consent. The Medical Ethics Committee of the University of Bochum approved the follow-up examination[2].

Telangiectasia assessment

Severity of telangiectasia was manually graded using a photonumeric 0-5 scale, as part of the SCINEXA[TM] method[3].

Determinants

BMI was assessed by physical examination. Information on skin color type (based on the Fitzpatrick scale[4]), household education level (highest level of education of the participants and their partners combined) and lifestyle (use of sun protection cream and sunbeds, holidays in sunny regions, smoking and alcohol consumption) was collected via interview.

Statistical analysis

In SALIA, we investigated the influence of lifestyle and physiological factors on telangiectasia using a multivariable linear regression model including age, BMI, skin type, use of sun protection cream and tanning beds, holidays in sun rich regions, smoking history, education level and alcohol consumption as independent variables. Information on these variables and on telangiectasia were available for 784 women and we included only these complete cases. The analysis was performed in R. A two-sided P-value of <0.05 was considered statistically significant.

RESULTS

Between May 2007 and March 2010, 834 women were screened on telangiectasia. A number of 50 women were excluded due to missing data, leaving 784 women included in the final analysis. The women were slightly older than in the RS with a mean age of 73.5 years (Supplementary Table S3). The mean value of the telangiectasia was 2.1.

The age range in the SALIA cohort was smaller (66-79 years) than the age range in the RS (51-98 years) and showed a decrease in telangiectasia with increasing age, whereas the RS showed an overall increase in telangiectasia with increasing age. However, when zooming in on the age range of 60-75 years in the RS, a decrease in telangiectasia was seen, similar to the SALIA cohort in the comparable age range (Supplementary Figures S1 and S2). Light skin color type (skin type I/II vs. III/IV: ß=0.44 [95%CI 0.22 to 0.66]) and smoking (current vs. never smoking: ß=0.66 [95%CI 0.002 to 1.33]) were replicated as potential determinants. Women using sun-cream protection showed less telangiectasia (ß=-0.21 [95%CI -0.45 to 0.02]). Age was associated with less telangiectasia (ß=-0.09 [95%CI -0.12 to -0.05], as opposed to the findings in the RS (Supplementary Table S4).

SUPPLEMENTARY TABLES AND FIGURES

Supplementary Table S1. Sensitivity analysis complete cases Rotterdam Study (N=1146)

Determinant	%Δ telangiectasia area[a]	95% CI	P-value
Sex			
male	ref	ref	ref
female	**19.0**	**[11.1 – 27.4]**	**0.008**
Age (per year)	**1.3**	**[0.7 – 2.0]**	**<0.001**
BMI (per point)	0.4	[-0.3 – 1.1]	0.243
Skin color			
white-to-olive	ref	ref	ref
white	8.8	[-0.6 – 19.1]	0.068
pale	**27.7**	**[12.6 – 44.9]**	**<0.001**
Baldness			
no/mild baldness	ref	ref	ref
moderate	-2.2	[-9.6 – 5.9]	0.588
extensive	2.9	[-6.9 – 13.8]	0.570
Tendency to develop sunburn	**14.0**	**[6.4 – 22.2]**	**<0.001**
Outdoor work history	2.0	[-5.6 – 10.3]	0.610
History of living in a sunny country	2.3	[-10.2 – 16.5]	0.733
Tanning bed use >10 times	-3.0	[-11.4 – 6.2]	0.508
Sun-protective behavior[b]	2.0	[-4.4 – 8.9]	0.550
Spending winter in sunny country	**-20.8**	**[-31.4 – -8.5]**	**0.002**
Smoking history[c]			
never	ref	ref	ref
former	**10.4**	**[2.9 – 18.3]**	**0.006**
current	**36.8**	**[25.2 – 49.5]**	**<0.001**
Education level[d]			
low	ref	ref	ref
medium	-2.8	[-13.2 – 8.9]	0.627
high	-5.3	[-16.1 – 7.0]	0.384
Alcohol (per glass per day)	4.0×10^{-4}	[-2.0 – 2.0]	0.999
Dry skin			
no	ref	ref	ref
yes	-1.2	[-7.2 – 5.3]	0.714
Batch[e]	**28.2**	**[16.5 – 41.0]**	**0.004**
Residual[f]	**2.2**	**[1.8 – 2.5]**	**<0.001**

Abbreviations: 95% CI, 95% conference interval; BMI, body mass index; ref, reference variable. Boldface indicates statistically significant determinants.

[a] %Δ: the percentage change in telangiectasia area (the % increase in the mean value of telangiectasia area per unit increase of the independent variable, calculated by the formula: $(\exp^{\beta}-1) \cdot 100\%$. E.g. 1.7% increase in telangiectasia area per 1 year of age; [b] wearing sunglasses and/or a brimmed hat in the sunshine; [c] cigars, cigarettes or pipe; [d] low (primary education); medium (lower secondary education/lower vocational education/intermediate vocational education); high (general secondary education/higher vocational education/university); [e] technical variable which accounts for possible changes in resolution; [f] technical variable which accounts for possible changes in flash light variability.

Supplementary Table S2. Sensitivity analysis women Rotterdam Study (N=1521)

Determinant	% Δ telangiectasia area[a]	95% CI	P-value
Age (per year)	**1.5**	**[1.1 – 1.8]**	**<0.001**
BMI (per point)	**0.6**	**[0.1 – 1.2]**	**0.034**
Skin color			
white-to-olive	ref	ref	ref
white	**10.2**	**[1.3 – 20.0]**	**0.024**
pale	**31.4**	**[16.2 – 48.7]**	**<0.001**
Baldness			
no/mild baldness	ref	ref	ref
moderate	2.4	[-3.8 – 9.1]	0.453
extensive	-3.3	[-12.5 – 7.0]	0.521
Tendency to develop sunburn	**7.8**	**[1.7 – 14.3]**	**0.012**
History of living in a sunny country	5.4	[-7.3 – 19.8]	0.424
Sun-protective behavior[b]	1.9	[-3.8 – 7.9]	0.524
Spending winter in sunny country	-7.7	[-18.7 – 4.8]	0.218
Smoking history[c]			
never	ref	ref	ref
former	**7.8**	**[1.7 – 14.3]**	**0.011**
current	**45.0**	**[33.7 – 57.3]**	**<0.001**
Education level[d]			
low	ref	ref	ref
medium	4.06	[-5.2 – 14.2]	0.401
high	1.7	[-8.4 – 13.0]	0.748
Alcohol (per glass per day)	0.9	[-1.5 – 3.3]	0.477
Dry skin			
no	ref	ref	ref
yes	-2.7	[-8.5 – 3.5]	0.388
Free androgen index[e]	0.8	[-1.3 – 2.8]	0.464
Estradiol (per pmol/l)	3.0×10^{-3}	[-0.01 – 0.02]	0.682
Batch[f]	**25.6**	**[14.5 – 37.9]**	**<0.001**
Residual[g]	**2.0**	**[1.7 – 2.4]**	**<0.001**

Abbreviations: 95% CI, 95% conference interval; BMI, body mass index; ref, reference variable. Boldface indicates statistically significant determinants.

[a] %Δ: the percentage change in telangiectasia area (the % increase in the mean value of telangiectasia area per unit increase of the independent variable, calculated by the formula: $(\exp^{\beta}-1) \cdot 100\%$. E.g. 1.7% increase in telangiectasia area per 1 year of age; [b]wearing sunglasses and/or a brimmed hat in the sunshine; [c]cigars, cigarettes or pipe; [d]low (primary education); medium (lower secondary education/lower vocational education/intermediate vocational education); high (general secondary education/higher vocational education/university); [e]free androgen index (calculated as total testosterone in nmol/l divided by sex hormone binding globulin in nmol/l); [f]technical variable which accounts for possible changes in resolution; [g]technical variable which accounts for possible changes in flash light variability.

Supplementary Table S3. Characteristics of 784 female participants of the SALIA cohort with telangiectasia measurements

Characteristic	Women N=784
Telangiectasia score - mean (SD)	2.1 (1.5)
Age at photo in years - mean (SD)	73.5 (3.0)
BMI in kg/m^2 - mean (SD)	27.3 (4.5)
Skin color	
I/II (%)	437 (55.7)
III/IV (%)	347 (44.3)
Regular use of sun protection cream	
no (%)	309 (39.4)
yes (%)	475 (60.6)
Tanning bed use	
never (%)	644 (82.1)
ever (%)	140 (17.9)
Holidays in sunrich regions in weeks per year – mean (SD)	1.4 (2.6)
Smoking history	
current (%)	21 (2.7)
former (%)	138 (17.6)
never (%)	625 (79.7)
Education level	
low: <10yrs education (%)	139 (17.7)
medium: 10yrs education (%)	385 (49.1)
high: >10yrs education (%)	260 (33.2)
Alcohol	
never (%)	130 (16.6)
ever (%)	654 (83.4)

Abbreviations: BMI, body mass index; SD, standard deviation.

Supplementary Table S4. Multivariable linear regression of facial telangiectasia: determinants of facial telangiectasia among 784 women of the SALIA cohort

Determinant	ß	95% CI	P-value
Age (per year)	**-0.09**	**[-0.12 – -0.05]**	**<0.001**
BMI (per point)	0.005	[-0.02 – 0.03]	0.714
Skin type (Fitzpatrick)			
III/IV	ref	ref	ref
I/II	**0.44**	**[0.22 – 0.66]**	**<0.001**
Regular use of sun protection cream			
no	ref	ref	ref
yes	-0.21	[-0.45 – 0.02]	0.074
Tanning bed use			
never	ref	ref	ref
ever	0.03	[-0.26 – 0.33]	0.827
Holidays in sunrich regions in weeks (per year)	-0.01	[-0.05 – 0.04]	0.797
Smoking history			
never	ref	ref	ref
former	0.20	[-0.09 – 0.48]	0.174
current	**0.66**	**[0.002 – 1.33]**	**0.049**
Education level			
low	ref	ref	ref
medium	-0.01	[-0.30 – 0.29]	0.958
high	-0.06	[-0.38 – 0.26]	0.701
Alcohol consumption			
never	ref	ref	ref
ever	0.003	[-0.29 – 0.29]	0.983

Abbreviations: BMI, body mass index; SD, ref, reference variable. Boldface indicates statistically significant determinants.
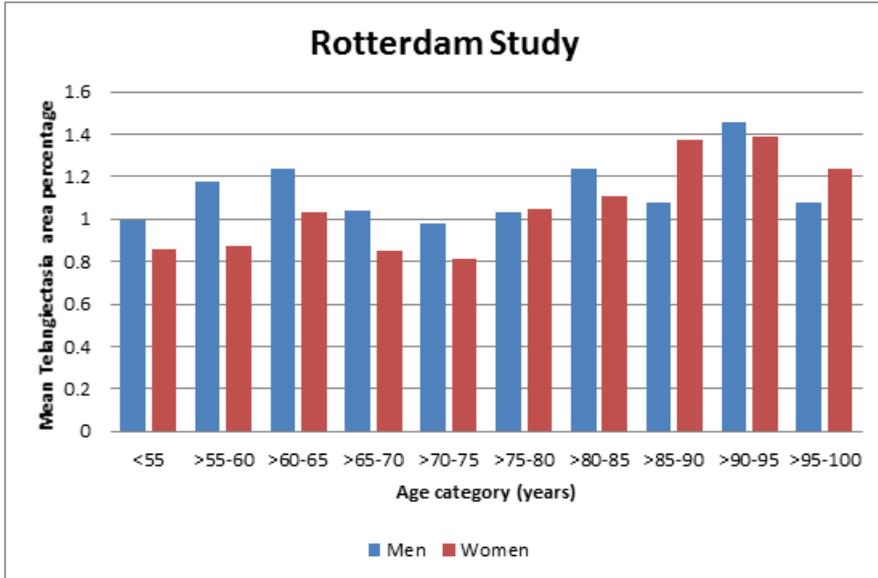
Supplementary Figure S1. Distribution of telangiectasia per age category in the Rotterdam Study.
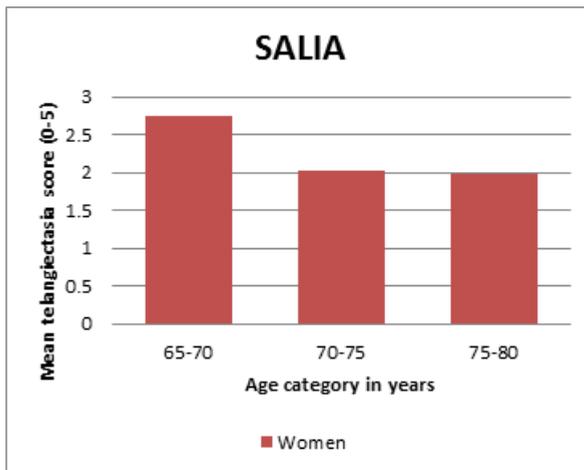
Supplementary Figure S2. Distribution of telangiectasia per age category in the SALIA cohort.

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