ORIGINAL PAPERS

Low sun exposure habits is associated with a dose-dependent increased risk of hypertension: a report from the large MISS cohort

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Abstract

In prospective observational cohort studies, increasing sun exposure habits have been associated with reduced risk of cardiovascular mortality. Our aim was to assess possible observational mechanisms for this phenomenon. A written questionnaire was answered by 23,593 women in the year 2000 regarding risk factors for melanoma, including factors of possible interest for hypertension, such as detailed sun exposure habits, hypertension, marital status, education, smoking, alcohol consumption, BMI, exercise, and chronic high stress. Hypertension was measured by the proxy "use of hypertension medication" 2005–2007, and high stress by "need of anti-depressive medication". Sun exposure habits was assessed by the number of `yes' to the following questions; Do you sunbath during summer?, During winter vacation?, Do you travel south to sunbath?, Or do you use sun bed? Women answering 'yes' on one or two questions had moderate and those answering 'yes' on three or four as having greatest sun exposure. The main outcome was the risk of hypertension by sun exposure habits adjusted for confounding. As compared to those women with the greatest sun exposure, women with low and moderate sun exposure were at 41% and 15% higher odds of hypertension (OR 1.41, 95% CI 1.3−1.6, $p < 0.001$ and OR 1.15, 95% CI 1.1−1.2, $p < 0.001$), respectively. There was a strong age-related increased risk of hypertension. Other risk factors for hypertension were lack of exercise (OR 1.36), a non-fair phenotype (OR 1.08), chronic high stress level (OR 1.8), and lack of university education (OR 1.3). We conclude that in our observational design sun exposure was associated with a dose-dependent reduced risk of hypertension, which might partly explain the fewer deaths of cardiovascular disease with increasing sun exposure.

Keywords Sun exposure · Cardiovascular disease · Hypertension · Risk factors · UV radiation

1 Introduction

An inverse association has been shown between cardiovascular disease (CVD) and vitamin D levels [1–3]. Chowedhury and coworkers estimated that 9.4% of all deaths in Europe and 12.8% in the US may be associated with vitamin D levels < 75 nmol/L [4]. However, prospective trials of vitamin D supplementation have not been able to show

benefit in terms of CVD [5]. However, the authors comment on several limitations of the studies such as no prespecified endpoint, underpowered and low doses [5]. In line with the latter, Afzal and coworkers used Mendelian randomization analysis to demonstrate that genotypes associated with low 25(OH)D levels were linked to a 14% increase in all-cause mortality for each 8 ng/mL lower vitamin D level, but not for CVD mortality [6]. Thus, there is a possibility that low vitamin D levels related to CVD might be a marker of something else.

It has been reported that at high latitudes women with active sun exposure habits have been associated with greater life expectancy, compared to those with inactive sun habits [7–9]. Compared to those with moderate and greatest sun exposure habits, women > 55 years of age with low sun exposure habits were at 1.5-fold and 2.3-fold, increased likelihood of death from CVD and one month shorter life expectancy per year [9, 10]. It was estimated that low sun exposure was a risk factor in the same magnitude as smoking

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for all-cause death [9]. Thus, in terms of CVD mortality, low vitamin D levels may be a marker of low sun exposure. Those with active sun exposure habits have sufficient vitamin D levels all year around, while those with inactive sun exposure are at low levels most of the year [11].

Feelisch and coworkers reported that UV radiation caused arterial vasodilatation resulting in a decrease in blood pressure [12]. Thus, UV radiation has been shown to lower transient blood pressure. It was hypothesized that CVD benefits of sunlight may be mediated by mechanisms other than vitamin D [12, 13]. However, it is still not known if individual sun exposure habits are related to persistent blood pressure or hypertension.

The aim of this study was to assess whether low sun exposure habits are associated with persistent high blood pressure as measured by the use of antihypertensive medication among those in the large prospective MISS cohort.

2 Materials and methods

2.1 Study design

The Melanoma in Southern Sweden (MISS) study was initiated in 1990. Our subjects consisted of approximately 1000 Sweden-born women of every age from 25 to 64 ($n=39{,}973$) who had no history of malignancy. The subjects were selected from the general population registry of the South Swedish Health Care Region by random computerized selection and represented 20% of the female population of South Sweden in the selected age groups. The women were invited to complete a standardized written questionnaire concerning risk factors for malignant melanoma. The initial inquiry was carried out from 1990 to 1992, and 29,518 women were subsequently enrolled in the study (response rate 74%).

A written follow-up inquiry was then conducted between 2000 and 2002. The questionnaire answered by 23,593, was a detailed inquiry into several factors of potential interest for blood pressure, such as sun exposure habits, marital status, educational level, smoking habits, alcohol consumption, use of combined oral contraceptives (COC), BMI, physical exercise, fair phenotype, and chronic high stress level.

We used background data from interview year 2000. We define hypertension as those who have been prescribed antihypertensive medication by their physician. In 2005–01–01 to 2007 all prescriptions filled in Sweden were recorded in the National Prescription Register. Those women with a prescription from Pharmaceutical Specialities Sweden (FASS) group; C02* (anti hypertension), C07* (beta blocker), C08* (calcium antagonists), or C09* (affecting renin-angiotensin system) were classified as having hypertension. Women who responded to the questionnaire during year 2000 and who had a prescription registered from 2005 to 2007 were included ($n=21{,}260$).

2.2 Sun exposure assessment

Four questions were asked regarding sun exposure: (1) how often do you sunbathe during the summertime? (never, $1-14$ times, $15-30$ times, >30 times); (2) Do you sunbathe during the winter, such as on holiday to the mountains? (no; $1-3$ days, $4-10$ days; >10 days); (3) Do you use tanning beds? (never; $1-3$ times/year; $4-10$ times/year; >10 times/year); and (4) Do you go abroad on holiday to swim and sunbathe? (never; once every 1–2 years; once/year; two or more times/year). The four questions were dichotomized into yes/no in the analysis (i.e. "no/never" or "sometimes"). As a measure of total sun exposure, sun exposure habits were categorized into three groups: zero "yes" responses (low sun exposure); "yes" response to one or two questions (moderate exposure); and "yes" response to three or four questions (greatest exposure).

2.3 Variable definitions

Smoking habits were recorded as smoker or nonsmoker. Weight and height were recorded and BMI was calculated in kg/m². BMI was classified into four groups: <25 (reference), 25 to <30 (overweight), ≥ 30 kg/m² (obese) and BMI missing. The level of regular exercise was categorized into three groups: none; walking at least once per week; or strenuous exercise (reference) such as cycling, swimming, gymnastics, or dancing $\geq$ once/week [14]. Women reporting having red hair or freckles were categorized as fair; other women were listed as non-fair. Women who had used COC for more than 5 years were classified as prior COC users. We classified those women on anti-depressant therapy as suffering from high chronic stress. Anti-depressive medication (i.e. having a FASS group N06A* prescription) is used for several condition such as; depression, burn out, and sleeping difficulties (when a high stress level is considered the cause). We believe that "chronic high stress level" is the shared characteristics for women on anti-depressive medication and use this classification.

The study was approved by the Ethics Committee of Lund University (LU 632-03).

2.4 Statistical analysis

Descriptive statistical analysis of the cohort who answered the year 2000 questionnaire was performed using cross-tabulation with a 95% confidence interval (CI) for those women with and without active sun exposure habits (Table 1). In Table 2 we present crude and adjusted logistic regression models for risk of hypertension. Hypertension

Table 1 Background variables and hypertension by sun exposure habits

| | Sun exposure habits | | | | | |
| | Low | | Moderate[a] | | Greatest[b] | |
	1904	%	12,938	%	6418	%
Age group (years)						
35–44	171	9.0	2630	20.3	1880	29.3
45–54	200	10.5	2956	22.8	2048	31.9
55–64	465	24.4	3447	26.6	1665	25.9
65–74	1068	56.1	3905	30.2	825	12.9
Exercise						
None	238	12.5	1138	8.8	398	6.2
Moderate	787	41.3	5940	45.9	2802	43.7
Strenuous	335	17.6	3734	28.9	2709	42.2
?	544	28.6	2126	16.4	509	7.9
Alcohol intake						
<5 g/day	857	45.0	2693	20.8	695	10.8
5–<15 g/day	726	38.1	6495	50.2	2874	44.8
>15 g/day	246	12.9	3663	28.3	2805	43.7
?	75	3.9	87	0.7	44	0.7
Fair phenotype	781	41.0	5431	42.0	2929	45.6
BMI						
<25	668	35.1	6530	50.5	4010	62.5
25–30	537	28.2	3848	29.7	1677	26.1
>30	337	17.7	1505	11.6	415	6.5
?	362	19.0	1055	8.2	316	4.9
Smoker	786	41.3	6823	52.7	3892	60.6
?	70	3.7	150	1.2	65	1.0
Prior COC >5 years	306	16.1	4002	30.9	2771	43.2
University school	463	24.3	4209	32.5	2629	41.0
Married	1220	64.1	9514	73.5	4927	76.8
Chronic stress	333	17.5	2144	16.6	1000	15.6

Hypertension (HT) as measured by "use of antiHT" medication 2005 to 2007

Chronic stress as measured by use of anti-depressant medication

prior COC Combined oral contraceptives at least 5 years, *?* Missing value

[a]Moderate sun exposure: answer yes to one or two of the following questions; Do you sunbath during summer?, during winter vacation?, do you travel south to sunbath?, or do you use sun bed?

[b]Greatest sun exposure: answering yes to three or four of the above questions

was used as a dependent variable; other selected variables were introduced as independent variables. Some independent variables were introduced because of their known relationships, such as age, smoking, and exercise level. Others were included if *p* values were less than 0.2 (alcohol consumption, university education, marital status, fair phenotype, prior use of COC, and chronic stress). Since BMI has been suggested as in the causal pathway of sun exposure, we predetermined to consider it only as a stratified variable [15]. Missing values were included in the adjusted analysis as a dummy variable. Thus, all cases were included in Tables 1 and 2, and no imputation was used. IBM SPSS 23 (Statistical Package for the Social Sciences, SPSS Inc., Chicago IL, USA) software was used for descriptive analysis and logistic regression analysis; *p* values < 0.05 were considered statistically significant.

3 Results

3.1 Background characteristics

In Table 1 we present the background characteristics of women with low, moderate and greatest sun exposure habits, i.e., having answered yes on zero, one or two, or three or four of the four sun exposure questions, respectively. Sun exposure habits differed in relation to most selected background variables.

Table 2 Risk of Hypertension by sun exposure habits

	Hypertension (HT)				Crude analysis		Adj analysis 1[a]		str analysis 2[b]		str analysis 3[c]	
	No	%	Yes	%	OR for HT		OR for HT		BMI < 25		BMI ≥ 25	
	n = 14,747		n = 6513		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Sun exposure[a]												
Low exposure	1007	6.8	897	13.8	3.0	2.7–3.4	1.41	1.3–1.6	1.4	1.1–1.7	1.5	1.1–2.0
Moderate	8773	59.5	4165	63.9	1.6	1.5–1.7	1.15	1.1–1.2	1.2	1.1–1.4	1.2	0.9–1.5
Greatest	4967	33.7	1451	22.3	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref
Age group year 2000[c] (years)												
35–44	4195	28.4	486	7.5	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref
45–54	4093	27.8	1111	17.1	2.3	2.1–2.6	2.5	2.2–2.9	2.7	2.1–3.5	2.5	1.8–3.5
55–64	3625	24.6	1952	30.0	4.6	4.2–5.2	4.6	4.1–5.2	4.7	3.6–6.0	4.3	3.1–5.9
65–74	2834	19.2	2964	45.5	9.0	8.1–10.0	8.2	7.2–9.4	9.3	7.3–11.8	6.1	4.4–8.4
Exercise												
None	1251	8.5	523	10.4	1.4	1.3–1.6	1.36	1.2–1.5	1.4	1.1–1.7	1.0	0.8–1.4
Moderate	6581	44.6	2948	58.8	1.5	1.4–1.6	1.31	1.2–1.4	1.3	1.1–1.5	0.9	0.7–1.2
Strenuous	5242	35.5	1536	30.7	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref
?	1673	11.3	1506	23.1	3.1	2.8–3.4	1.35	1.2–1.5	1.39	1.1–1.5	1.14	0.9–1.5
Alcohol intake												
< 5 g/day	2514	17.0	1731	26.6	1.6	1.4–1.7	1.19	1.1–1.3	1.1	0.9–1.2	1.1	0.9–1.4
5–< 15 g/day	7000	47.5	3095	47.5	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref
> 15 g/day	5109	34.6	2518	38.7	0.7	0.7–0.8	0.9	0.8–1.0	1.1	0.9–1.2	1.1	1.0–1.2
?	124	0.8	82	1.3	1.5	1.1–2.0	1.14	0.8–1.6	1.38	0.8–2.4	0.83	0.3–2.5
Non-fair phenotype	8124	55.1	3995	61.3	1.3	1.2–1.4	1.08	1.01–1.15	1.1	1.0–1.2	1.1	1.0–1.4
High stress	2243	13.2	1234	18.9	1.3	1.2–1.4	1.80	1.4–2.3	2.5	1.6–3.8	1.2	0.7–2.2
University	5495	37.3	1806	27.7	0.6	0.6–0.7	0.79	0.7–0.8	0.9	0.8–1.0	0.9	0.7–1.0
BMI[b]												
< 25	8607	58.4	2601	39.9	1.0	Ref			Included			
25–30	3920	26.6	2142	32.9	1.8	1.7–1.9					Included	
> 30	1218	8.3	1039	16.0	2.8	2.6–3.1					Included	
?	1002	6.8	731	11.2	2.41	2.2–2.7						
Smoker	8313	56.4	3188	48.9	0.7	0.7–0.8						
Married	11,018	74.7	4643	71.3	0.8	0.8–0.9						
Prior COC > 5 years	5548	37.6	1531	23.5	0.5	0.5–0.5						

Since BMI has been suggested to be in the causal pathway between sun exposure and CVD it was predetermined to only be presented in stratified analysis

[a]Adjusted for all shown variables shown in column, *Str* stratified, ? Denotes missing data

[b]Adjusted as above among non-overweight

[c]Adjusted for same variables as model 1 only among those with BMI > 25

3.2 Outcome

In Table 2 we present the selected variables in relation to hypertension, together with crude ORs and three adjusted models. The main outcome is presented in adjusted model 1. Women with low and moderate sun exposure habits were at 41% and 15% higher odds of hypertension, respectively, as compared to those with greatest sun exposure habits (model 1, Fig. 1). As expected there is a strong relationship between increasing age and the odds of hypertension. Also, women with chronic high stress were at almost double risk

of hypertension (OR 1.8, 95% CI 1.4−2.3). Women who did not exercise were at a 36% increased association to hypertension (OR 1.36, 95% CI 1.2−1.5) (Fig. 1). In our modeling smoking, marital status and prior use of COC were not significantly related to hypertension. We tested for interactions and found an interaction between age group and high stress; this interaction was included in models 1 to 3. When high stress was introduced, OR for hypertension increased from OR 1.4, 95% CI 1.3−1.6 to OR 1.8, 95% CI 1.8−2.8. The OR of overweight (1.5, 95% CI 1.4–1.6) and obesity (2.4, 95% CI 2.1−2.6) for hypertension are not included in model
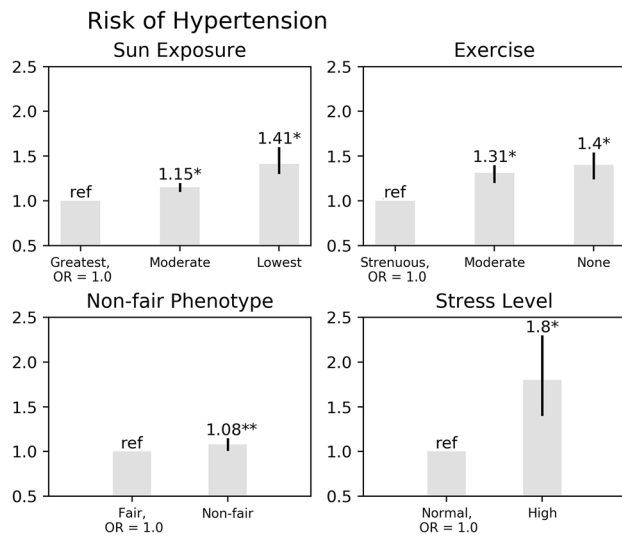
Risk of Hypertension

Fig. 1 Risk of hypertension. As compared to greatest sun exposure, moderate and low sun exposure were related to 15% and 41% increased odds of hypertension. As compared to strenuous exercise moderate and no exercise were related to 31% and 40% increased odds of hypertension. Women with Non-fair and those with a high stress level were at 8% and 80% increased odds of hypertension. *Denotes significance of difference $p < 0.001$, **$p = 0.02$

1, but data are given stratified in model 2 and model 3. The OR of women with BMI < and ≥ 25 were similar as the OR in model 1, but with a wider CI.

In Supplementary Table 1 we show the same data as Table 2, adjusted analysis 1 also including BMI in model 1, in model 2 including all women who answered the questionnaire. Finally in model 3, we include the same data as Table 2, model 2, but excluding participants with missing variables.

4　Discussion and conclusion

In this study we find an inverse dose-dependent association between sun exposure habits and hypertension, adjusted for possible covariates. We sought to assess if the lower CVD mortality associated with active sun exposure habits might be mediated through a persistent reduction in blood pressure, which was found. Although our findings are of an observational nature, they lend some support to the hypothesis that low vitamin D levels in relation to CVD might be a marker of low sun exposure, and not the mediator of hypertension. Thus, this could explain why vitamin D supplementation does not seem to affect the risk of CVD. In addition, lack of exercise, increasing stress, and having a non-fair phenotype were related to a significantly increased OR for hypertension.

In agreement with our findings, a Chinese study reported that women who sunbathed 30 min per day had a 40% lower risk of hypertension [16]. In a Saudi Arabian study, the risk of hypertension decreased from 28.1 to 11.1%, blood pressure decreased from a mean of 118.3/76.0–112.6/73.9 and the mean BMI dropped, with recommendation of increased dietary vitamins and 5–30 min of sun exposure twice a week for 1 year. The sun exposure was recommended before 10 o'clock or after 14, i.e., when the UV index was not high (UV index > 6) [17]. Two studies report an inverse relationship between ambient UV radiation and systolic blood pressure [18, 19]. The US study found a 59% increased risk of stroke in areas below the median of ambient UV radiation, as compared to above [18]. Blood pressure was reported to be independent of vitamin D [18, 20]. A recent study comprising dialysis patients in the US shows that higher incident UV radiation, to be associated with lower blood pressure [21]. There are several interventional studies assessing the effect of UVA and/or UVB light on the effect on transient blood pressure. There seems to be a transient effect resulting from UV radiation, but studies to date have been small and have had divergent results [12, 22–25].

4.1　Possible mechanisms that may explain the relationship between sun exposure and the lower risk of CVD mortality

Liu and co-workers reported that large stores of nitrogen oxides (NO) mobilized into the systemic circulation in response to UV radiation lowered blood pressure, a finding that was reportedly independent of temperature and vitamin D [12]. Since hypertension is a major risk factor for stroke and myocardial infarction, a plausible reason for the sun exposure associated reduced CVD mortality might be a mediating vasodilator effect of NO, which in turn reduces blood pressure. Lack of exercise is a known risk factor for both hypertension and CVD [26]. In addition, both exercise and sun exposure increase sweating, which contain sodium chloride. A low salt status is related to lower blood pressure, and a lower risk of hypertension [27]. It is not possible to differentiate active sun exposure habits from a healthy lifestyle with more activity and less overweight. However, smoking and alcohol consumption was higher. Hypertension is a major driver for the global burden of disease, especially for myocardial infarction and stroke. If sun exposure does affect long-term blood pressure, it may be a modifiable risk factor [28, 29]. In our observational design, sun exposure is associated with lower incidence of several of the major common diseases such as; type 2 diabetes mellitus, thromboembolism, hypertension, CVD, and non-CVD/non-cancer mortality [9, 14, 30].

Sun exposure also have an anxiolytic effect by endorphin release [31]. Chronic stress has been shown to cause

endothelial dysfunction, hypertension, and atherosclerosis [32–34]. A randomized trial comprising vitamin D-deficient depressed individuals showed a reduction from 24 to 13 on the Beck Depression Inventory by prescribing safe sun exposure and activating exercise for 12 weeks [35]. Thus, approximately half of those in the study participants were cured at time point 2, while the control group remained at a mean score of 23. Whole body UV exposure for dermal conditions improved the Montgomery Åsberg Depression Rating Scale (MADRS) significantly after 6 weeks as compared to control group receiving placebo light [36]. Lack of endorphin may cause the activation of sympathetic nerves resulting in increased stress. It has recently been shown that melanocytic stem cells were prematurely depleted in response to high stress causing decoloration of the hair [37]. In accordance with above, our data show that women with a high chronic stress level were at a doubled risk of hypertension.

Blacks have a higher prevalence of hypertension at 55 years of age as compare to whites [38]. We find non-fair Caucasian women to be at an 8% increased risk of hypertension compared to fair (Table 2). Although we compared different shades of white, the finding of an inverse association between fair phenotype and the risk of hypertension is in agreement with the reported survival advantage of fair skin in a low UV milieu, including a 59% increased risk of death due to skin cancer [39]. Thus, assuming causality, the increased risk of death due to skin cancer might be interpreted as the "price" for a survival advantage in a low UV region.

It is not always possible to differentiate between the effects of cold and low UVR, but cold has been reported to upregulate central angiotensin receptors [40]. In order to increase body temperature in cold weather, the sympathetic nervous system and hypothalamic-pituitary–adrenal axis may be activated. Activation of the renin–angiotensin–aldosterone system will cause sodium and water retention [40]. A Japanese study reported that low solar radiation was associated with a substantial attributable risk for outside-hospital cardiac arrest [41]. Similarly, an increased risk of acute coronary events, stroke, and venous thromboembolism has been reported in winter [30, 42, 43]. Thus, the winter peak of CVD events may at least partially be explained by higher blood pressure due to a combination of cold and low UV exposure [44]. Preeclampsia is characterized by hypertension and proteinuria. The prevalence of eclampsia is almost doubled during the winter season in Sweden [45].

4.2 Strengths and limitations

It is a strength that our large cohort was drawn randomly from the Swedish population register for 1990. A drawback is that we do not know if all women with hypertension were diagnosed and treated with anti-hypertension medication or how many who had hypertension at inception. However, sun exposure habits tend to be quite constant [46]. In addition, some women will be prescribed a b-blocker for indications other than hypertension. However, we believe that our data will be valid on a group level. All findings are of observational type and may not be causal. We have relied on a single occasion assessment of sun exposure, which might cause bias. However, such a bias usually tends to underestimate differences [47]. We included only women receiving a prescription during 2005–2007. Thus, severely ill women who were in hospital or geriatric departments, or who died before 2005 were not included. Also, those who were most healthy and not taking prescription medicine were not included. Since we used different inclusion criteria with almost identical ORs (supplementary Table 1), we believe the results of Table 2 model 1 give the most accurate results.

We conclude that increased sun exposure seems to be associated to a dose-dependent reduced risk of hypertension, which at least in part may mediate the lower CVD mortality observed among those with greater sun exposure habits. This does not rule out other possible mechanisms, such as reduced stress or altered glucose metabolism by sun exposure.

Compliance with ethical standards

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