Sleep duration and cardiovascular risk: results of the large-scale epidemiology study ESSE-RF

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Abstract

Background. The recent data suggest that sleep disorders are associated with cardiovascular diseases. We assessed the relation between self-reported sleep duration and cardiovascular and metabolic disorders in the large-scale epidemiological study.
Material and methods. The ESSE-RF is a population-based cross-sectional study involving 22,258 participants aged 25–64 years from 13 regions of the Russian Federation. In 2012–2014, all subjects underwent a structured interview including questions about average daily sleep duration, lifestyle, complaints and diseases. The current analyses considered the associations with the following disorders: obesity, hypertension, coronary artery disease, myocardial infarction, stroke (cerebral thrombosis or hemorrhage) and diabetes mellitus.
Results. Altogether 20,359 respondents were included in the final analysis. The mean self-reported sleep duration was 7.0 h per night: 23.3% participants reported sleeping less than 6 h while 4.5% subjects slept more than 9 h. We found both short and long sleep duration to be associated with self-reported cardiovascular diseases. The association was independent of age, sex, body mass index, blood pressure, lipids and glucose levels. The multivariable odds were higher for obesity in short-sleepers compared to those sleeping 7–8 h. In the meanwhile, the association was U-shaped for coronary artery disease. A J-shaped relation was found for myocardial infarction. No relation was found for hypertension, diabetes mellitus or stroke.
Conclusions. Differences in sleep duration may have health consequences given associations between short and long sleep duration and cardiometabolic outcomes.
Key words: epidemiology; obesity; sleep; risk factors; cardiovascular diseases

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Introduction

Increasing evidence indicates that sufficient sleep duration and sleep quality are important for the primary and secondary cardiovascular prevention [1, 2]. The leading sleep medical associations recommend 7–9 hours of daily sleep for adults [3–5]. The association between the cardiovascular event risk and sleep duration is characterized by the U-shape curve which implies different mechanisms affecting prognosis in the long- and short-sleepers [6]. Moreover, the majority of cross-sectional and observational studies show an increased rate of obesity, cardiovascular diseases, stroke and mortality in subjects with poor sleep quality, as well as in short- and long-sleepers [7]. A number of experimental studies showed that short sleep is potentially associated with the adverse endocrine, immune, and metabolic effects. However, the underlying mechanisms remain unclear. Nevertheless, the following mechanisms are discussed: sympathetic activation, disruption of energy balance, proinflammatory state, impaired insulin sensitivity, enhancement of lipid metabolism abnormalities, etc. [8–10]. Experimental studies demonstrated blood pressure elevation after one night of partial sleep deprivation [11] and its decline after sleep prolongation [12]. All these factors are known to be involved in the cardiovascular continuum promoting atherosclerosis progression and increasing risk of cardiovascular events [4]. Some authors indicate that different sleep duration and sleep disturbances might be associated with different outcomes. Thus, CARDIA study showed that long sleep duration is mostly associated with increased risk of dyslipidemia [13]. Cross-sectional and prospective studies demonstrated that the prevalence of stroke and myocardial infarction (MI) is higher in both short and long sleepers, but the sleep debt mostly increases risk of MI [7, 14].

Complaints related to short sleep and poor sleep quality are more often reported by elderly people. Some studies showed that these changes are more frequent and start earlier in women than in men [15]. Moreover, based on the Whitehall II Study, only in women short duration of sleep is associated with higher risks of hypertension. The gender-related differences are mostly explained by the effects of sex hormones, and in particular major hormonal shifts more pronounced in women than in men. At the same time, psychosocial and behavioral factors can also have an impact on sleep characteristics in men and women [16].

The multicenter study "Epidemiology of cardiovascular disease in different regions of the Russian Federation — ESSE-RF" is the first epidemiological study to evaluate the sleep duration among Russians [17]. The main objective of this epidemiological study was to study the prevalence of risk factors and cardiovascular diseases in 13 regions of the Russian Federation (RF) with different climate, geographic, economic and demographic characteristics, to elaborate the risk model for Russian population, and to investigate the traditional and new cardiovascular risk factors. We hypothesize that short and long sleep can be one of the new possible risk factors for cardiovascular diseases (CVD).

The aim of this cross-sectional analysis was to investigate the relationship between self-reported sleep duration and various cardiovascular and metabolic disorders.

Material and methods

A representative population-based sample of male and female individuals aged 25 to 64 years old was enrolled from 13 Russian regions and cities (North Ossetia — Alania Republic (North Caucasus), Volgograd (South), Vologda (North-West), Voronezh (Centre), Ivanovo (Centre), Kemerovo (West Siberia), Krasnoyarsk (East Siberia), Orenburg (Volga region), Vladivostok (Far East), St Petersburg (North West), Tomsk (West Siberia), Ekaterinburg (West Siberia), Tyumen (Ural)). The survey was accomplished within the period from November 1, 2012 to November 25, 2014. The study was approved by the Institutional Review Boards of 3 main centers: Almazov National Medical Research Centre (St Petersburg), National Research Center for Preventive Medicine (Moscow), Russian Cardiology Research and Production Complex (Moscow) and the associate centers. Detailed study design and enrollment process were described previously elsewhere [17]. All participants gave written informed consent. The response rate was on average 80%.

Overall, 22,258 participants underwent the ESSE-RF survey (8541 men, 38.4%). Out of all included subjects, 1899 (8.5%) respondents were excluded due to the missing data: lab tests (n = 887), sleep module (n = 542); inconsistent data (n = 289); 112, 16 and 53 did not report their height, weight and waist/hip ratio, respectively. Therefore, in total 20,359 respondents were included in the final analysis [7,746 men, 38%; mean age — 48 (25; 64) years].

All subjects underwent a structured interview. The questionnaire was designed on a modular type and included questions regarding social and demographic characteristics, life style and habits (including cigarette smoking, alcohol consumption and physical activity), anamnesis, etc. in accordance with the adapted international methods. Alcohol abuse was considered when ≥ 168 g of ethanol per week was consumed by men and ≥ 84 g of ethanol per week by women. The level of physical activity was considered low when a subject reported less than 150 minutes of moderate or less than 75 minutes of intense aerobic physical activity per week, which is the recommended minimum level for adults (walking at medium or high speed, or any other equivalent activity) [18].

History was recorded in the module "diseases" by answering the question "Have your doctor ever told that you have/had the following diseases?" followed by the list of 17 pathologies. In the present paper, we analyzed hypertension, coronary artery disease (CAD), myocardial infarction (MI), stroke (cerebral thrombosis or hemorrhage), obesity, and diabetes mellitus (DM). Participants were asked to provide information about average sleep duration in hours (during one month before the survey): "What was your daily sleep duration? Please, include the naps". Sleep duration of 6 hours or less was considered short [19], ≥ 9 hours was considered long [20]. Physical examination included anthropometric measurements (waist circumference, height, and weight). Body mass index (BMI) was calculated by Quetelet index — body weight [kg]/height^2 [m^2]. Obesity was diagnosed in case of BMI ≥ 30 kg/m^2. Hypertension was considered when office systolic blood pressure (SBP) was ≥ 140 mm Hg and/or diastolic blood pressure (DBP) was ≥ 90 mm Hg or antihypertensive therapy was ongoing at the time of the survey. Blood samples were collected according to standardized protocols after ≥ 12-hour fasting on the day of the survey before the interview and anthropometric measurements were taken. Blood samples were centrifuged at low speed 900 g for 20 minutes at +4°C. Serum was immediately frozen and stored at temperature below –20°C until they were transferred by special logistic services to the laboratory at the responsible participating center.

The following parameters were evaluated: total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), triglycerides, glucose, creatinine, uric acid (Abbot Architect c8000, USA). Glomerular filtration rate (GFR) was estimated by the formula CKD-EPI [21].

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics v.21 (USA). Each parameter was tested for normal distribution using the Kolmogorov-Smirnov test. In case of normal distribution the parameters are presented as mean and standard deviation. In case of non-normal distribution the parameters are presented as median and range (minimum; maximum). Comparative analysis of the quantitative variables was performed using Student's t-test. Fisher's exact test and χ^2 were used for categorical variables. ANOVA was applied for multiple comparisons. Logistic regression analysis was used to determine predictors among categorical parameters. Sleep duration was included as dependent variable. Cardiovascular diseases (hypertension, CAD etc.), metabolic disorders and other traditional risk factors (age, BMI, office SBP and DBP, smoking, alcohol overuse, cholesterol levels, fasting glucose etc.) were included as independent variables in the univariate analysis. Those factors that had significant predictive value ($p < 0.05$) in the univariate analysis were included in a multivariate model (multinomial logistic regression). Closely correlated factors were not included in the same analysis (e.g. BMI in obesity analysis, glucose level in DM analysis etc.). We estimated odds ratios (ORs) and 95% confidence intervals (95% CI) for sleep parameters associated with each risk factor and disorder. Direct standardization of data reported from each region was performed according to the European standards. Differences were considered significant at p-level < 0.05.

Results

Mean sleep duration was 7 (1; 16) hours. The life style characteristics were as following: 4440 (21.8%) smokers, 674 (3.3%) subjects reported alcohol abuse, low physical activity (less than 5 times a week) — 14209 (69.8%) respondents. About one third of subjects (n = 7175, 35%) were overweight (25 ≤ BMI < 30 kg/m^2), every fifth respondent (n = 4287, 21%) had obesity I degree, the rate of obesity II and III degree was significantly lower (n = 1609, 8% and n = 722, 4%, respectively). Every 20th patient (n = 939, 5%) had weight deficit (BMI <19.9 kg/m^2). Normal fasting glucose level was found in 14961 (74%) participants, while 2323 (11%) participants had impaired fasting glucose. Diabetes mellitus was newly diagnosed (based on fasting plasma glucose) in 1960 (10%) patients, while 968 (5%) participants reported previously diagnosed DM. All the subjects were divided into groups based on the sleep duration for the last month: ≤ 6 hours, 6 < sleep < 7 hours, 7–8 hours, 8 < sleep ≤ 9 hours and > 9 hours of sleep (Tab. I). The majority of subjects reported 7–8 hours (33.3%) and from 6 to 7 hours (32.6%) of sleep

Table I. Clinical and demographic characteristics of the study participants depending on sleep duration (n = 20359)

Variable	All	≤ 6 hours	6 < sleep < 7 hours	7–8 hours	8 < sleep ≤ 9 hours	> 9 hours	p
Age (years)	48 (25; 64)	50 (25; 64)	48 (25; 64)	48 (25; 64)	47 (25; 64)	46 (25; 64)	< 0.001
25–34 n = 4304 (%)	21.1	20.8	33.6	33.08	6.78	5.62	χ^2 = 84.822 p < 0.001
35–44 n = 4078 (%)	20	20.57	34.69	34.69	6.2	4.36	
45–54 n = 5681 (%)	27.9	24.55	32.7	33.25	5.42	4.01	
55–64 n = 6296 (%)	30.9	25.84	30.5	30.54	6.25	4.3	
Gender, men/women n (%)	7746 (38%) 12613 (62%)	1714 (22.1%) 3045 (24.1%)	2590 (33.4%) 4057 (32.1%)	2695 (34.8%) 4092 (32.4%)	424 (5.4%) 823 (6.5%)	323 (4.1%) 596 (4.7%)	χ^2 = 30.6; < 0.001
BMI [kg/m^2]	27.4 (15; 68)	27.8 (15; 68)	27.0 (15; 59)	27.4 (15; 54)	27.0 (15; 53)	27.0 (16; 51)	< 0.001
Waist circumference [cm] Men, Women	92 (41; 160) 85 (44; 160)	92 (55; 150) 87.5 (44; 160)	92 (52; 152) 85 (50; 160)	92 (41; 160) 86 (45; 143)	92 (48; 135) 84 (57; 35.5)	93 (60; 134) 85 (56; 146)	< 0.05 < 0.001
SBP [mm Hg]	131 (83; 233)	131 (87; 240)	130 (80; 240)	130 (79; 240)	127 (85; 222)	128 (83;240)	< 0.001
DBP [mm Hg]	81 (48; 137)	81 (47;150)	81 (40; 146)	81 (40; 150)	80 (48; 134)	81 (44;130)	< 0.001
HR [beat per min]	73 (42; 153)	73 (43;150)	73 (41; 165)	73 (42; 135)	73 (45; 132)	73 (43;128)	0.042
Obesity n = 6648 (%)	33	36.3	31.7	31.8	30.8	32.9	χ^2 = 34.5; p < 0.001
DM (history) n = 968 (%)	4.7	5.4	4.4	4.5	5.1	5.2	χ^2 = 7.2; p = 0.13
Hypertension n = 7670 (%)	38	40.8	36.7	37.1	34	37.6	χ^2 = 30; p < 0.001
CAD n = 2116 (%)	10.0	13.4	8.7	9.7	10.3	11.9	χ^2 = 70.6; p < 0.001
MI n = 443 (%)	2.2	2.6	1.7	2.2	2.6	2.8	χ^2 = 15.8; p = 0.003
Stroke n = 422 (%)	2.1	2.2	1.9	2.2	2.4	1.6	χ^2 = 4.2; p = 0.4
Smoking n = 4440 (%)	21.8	24.1	21.9	20.1	18.9	24.7	χ^2 = 37.4; < 0.001
Alcohol abuse n = 674 (%)	3.3	3.2	3.2	3.2	4.1	4.2	0.2
Low physical activity n = 14209 (%)	69.8	57.3	71.6	70.0	77.4	59.4	χ^2 = 24.3; < 0.001

BMI — body mass index; CAD — coronary artery disease; DBP — diastolic blood pressure; DM — diabetes mellitus; MI — myocardial infarction; SBP — systolic blood pressure

daily. Almost every 4th participant reported usual short sleep (23.3%), while only 4.5% were long-sleepers. The similar distribution was found both in men and women. Subjects with longer sleep duration (> 9 hours) were younger compared to those sleeping ≤ 6 hours. Prevalence of short-sleepers increased in elder subjects.

Those sleeping > 8 hours had the lowest BMI, while short-sleepers had higher BMI values. SBP also increased in short sleepers. Heart rate, glucose and creatinine levels and GFR were also associated with sleep duration, while no significant relation was found between sleep duration and total cholesterol, LDL or triglycerides (Tab. II). At the same time

Table II. Laboratory parameters of the study participants depending on sleep duration (n = 20,359)

Variable	All	≤ 6 hours	6 < sleep < 7 hours	7–8 hours	8 < sleep ≤ 9 hours	> 9 hours	p
Cholesterol [mmol/L]	5.4 (1.7; 15.7)	5.3 (2.1; 14)	5.3 (2.2; 11)	5.3 (2.1; 12)	5.3 (2.4; 10)	5.3 (2.2; 16)	0.64
LDL [mmol/L]	3.3 (0.5; 12.1)	3.3 (0.5; 10)	3.3 (0.6; 8.6)	3.3 (0.7; 8.9)	3.3 (1.0; 7.3)	3.2 (0.8; 12)	0.06
HDL [mmol/L]	1.4 (0.2; 3.8)	1.4 (0.4; 3.8)	1.4 (0.4; 3.9)	1.4 (0.2; 3)	1.4 (0.5; 2.8)	1.3 (0.4; 3)	0.015
Triglyceride [mmol/L]	1.2 (0.1; 16.1)	1.2 (0.1; 14)	1.2 (0.1; 16)	1.2 (0.2; 16)	1.2 (0.3; 10)	1.2 (0.3; 19)	0.15
Glucose [mmol/L]	5.1 (2.5; 25.5)	5.1 (2.5; 24)	5.1 (2.5; 25.5)	5.1 (2.7; 22.5)	5.0 (3; 24)	5.1 (2.6; 21)	0.024
Creatinine [μmol/L]	69.3 (31; 918)	67.0 (33; 734)	67.4 (31; 700)	68.0 (32; 653)	67.0 (39; 461)	67.0 (41; 918)	0.022
GFR [μmol/L/min × 1.73]	100 (5.4; 173)	99.5 (7; 152)	100.4 (7; 173)	100.0 (6; 166)	100.5 (9; 138)	100.0 (5; 138)	0.021
Uric Acid, [mmol/L] Men/Women	346 (81; 1000) 270 (80; 1130)	340 (110; 800) 270 (80; 777)	350 (100; 1000) 270 (80; 1030)	341 (81; 850) 267 (80; 925)	344 (163; 650) 260 (110; 1130)	330 (126; 810) 260 (89; 676)	< 0.05 > 0.05

HDL — high density lipoprotein; GFR — glomerular filtration rate; LDL — low density lipoprotein

Table III. Association between sleep duration and cardiovascular diseases (OR; 95% CI)

Sleep duration		Obesity	Diabetes Mellitus	Hypertension	Coronary Artery Disease	Myocardial Infarction	Stroke
≤ 6 h	Model 1	1.2*** (1.1; 1.3)	1.2* (1.02; 1.4)	1.2*** (1.1; 1.3)	1.4*** (1.3; 1.6)	1.2 (0.9; 1.5)	1.0 (0.8; 1.3)
	Model 2	1.1** (1.04; 1.3)	1.0 (0.9; 1.2)	1.1 (1.0; 1.2)	1.3*** (1.2; 1.5)	1.1 (0.9; 1.5)	0.9 (0.7; 1.2)
6 < sleep < 7 h	Model 1	1.0 (0.9; 1.1)	1.0 (0.9; 1.2)	1.0 (0.9; 1.1)	0.8* (0.7; 0.9)	0.7* (0.6; 0.9)	0.9 (0.7; 1.1)
	Model 2	1.0 (0.9; 1.1)	1.0 (0.9; 1.2)	1.0 (0.9; 1.1)	0.9 (0.8; 1.0)	0.8 (0.6; 1.0)	0.9 (0.7; 1.1)
7–8 h		Reference variable					
8 < sleep ≤ 9 h	Model 1	1.0 (0.8; 1.1)	1.1 (0.9; 1.5)	0.8* (0.7; 0.9)	1.1 (0.9; 1.3)	1.2 (0.8; 1.7)	1.1 (0.7; 1.7)
	Model 2	1.0 (0.9; 1.2)	1.2 (0.9; 1.6)	0.9 (0.8; 1.1)	1.1 (0.9; 1.4)	1.3 (0.9; 2.0)	1.2 (0.8; 1.8)
> 9 h	Model 1	1.0 (0.9; 1.2)	1.2 (0.9; 1.6)	1.0 (0.9; 1.2)	1.3* (1.02; 1.6)	1.3 (0.8; 2.0)	0.8 (0.4; 1.3)
	Model 2	1.1 (0.9; 1,3)	1.3 (0.9; 1.8)	1.1 (1.0; 1.3)	1.5** (1.1; 1.8)	1.6* (1.02; 2.4)	0.8 (0.5; 1.4)

Model 1 — unadjusted; Model 2 — adjusted for sex, age, body mass index, office blood pressure, smoking and low physical activity; *p < 0.05; **p < 0.01; ***p < 0.001

HDL cholesterol was significantly lower in long-sleepers. Gender-specific differences were shown for uric acid: the highest levels of uric acid were found in men sleeping 6–7 hours.

Short- and long-sleepers less often had low physical activity (χ^2 = 24.3; p < 0.001) and smoked more often (χ^2 = 37.4; p < 0.001) than normal sleepers. The rate of alcohol abuse was not significant in groups with different sleep duration.

We also found (Tab. I) a U-shaped relation between sleep duration and other cardiovascular risk factors and diseases: short- and long-sleepers had higher incidence of obesity, hypertension, CAD and MI. There were no significant differences for DM and stroke.

Logistic regression showed a higher probability of obesity, hypertension and CAD (Tab. III) in short-sleepers. Six-to-seven-hour sleep was associated with lower probability of CAD and MI. Moreover, sleep duration from 8 to 9 hours was associated with the lowest risk of hypertension (OR = 0.8; CI: 0.7–0.9, p = 0.037). At the same time sleep over 9 hours was associated with the higher risk of CAD (OR = 1.3; CI: 1.02–1.6, p = 0.043). After adjustment for sex, age, BMI, office blood pressure, smoking and low physical activity the associations were weaker but remained significant (Tab. II). Compared with subjects sleeping 7–8 h, the multivariable OR (95% CI) was higher for obesity in short-sleepers — 1.1 (1.03; 1.2), meanwhile the association was U-shaped for CAD, and J-shaped for MI. No associations were found for hypertension, DM and stroke.

Discussion

Based on the data from the epidemiological study ESSE-RF the median sleep duration in Russian citizens is 7 hours. Almost every 4th citizen (23.3%) is a short-sleeper. This conforms with the results of the National Health Interview Survey [22] — 29% (8% subjects sleeping ≤ 5 h/day and 21% those sleeping 6 h/day), but the prevalence of short-sleepers among Russian population is significantly higher than the data reported in the Sleep Heart Health Study (9.2%) [23]. These differences are due to the various approaches for sleep assessment. The first study, similarly to ours, estimated average daily sleep duration, while the second one identified mean sleep duration on weekends and workdays. In both studies, the proportion of long-sleepers is greater than in our cohort — 4.5% *vs.* 7.6% and 9% in SHHS and NHIS, respectively.

Based on our analysis, short sleep duration is associated with the increased risk of obesity, hypertension and CAD. The incidence of CAD and MI was higher for both short- and long-sleepers. No significant differences between subjects with various sleep duration were found regarding alcohol abuse. However, short- and long-sleepers reported lower prevalence of low physical activity and smoked more frequently. Therefore, our data do not confirm any definite and unidirectional relationship between sleep duration and cardiovascular risk factors.

The data on sleep duration and sleep quality in Russian population is lacking. The ESSE-RF is the first study which estimated sleep duration in Russia. At the same time, sleep quality was assessed in few other studies. Participants of the HAPIEE study 45–69 years old reported frequent spontaneous sleep interruptions in 20%; and unsatisfying sleep in 10% respondents [24]. Sleep quality was associated with angina, arthritis and depression in the analysis of the data from Russian population performed by the SAGE investigators [25].

Unlike other studies, our analysis did not show associations between short or long sleep duration with DM, hypertension or stroke. The Sleep Heart Health Study demonstrated higher risk for hypertension [23] for both short- (OR = 1.66, CI 1.35–2.04, p < 0.0001) and long-sleepers (OR = 1.30, CI: 1.04–1.62, p < 0.0001). In addition, both short-sleepers (OR = 2.01, CI: 1.5–2.70, p < 0.005) and long-sleepers (OR = 2.22, CI: 1.69–2.91, p< 0.005) had higher risk of stroke [19]. The meta-analyses of 24 prospective cohorts including 474 684 participants with short (≤ 5–6 h) (OR = 1.15, CI: 1.00–1.31, p = 0.047) and long sleep duration (> 8–9 h) (OR = 1.65, CI: 1.45–1.87, p < 0.0001) showed higher risk of fatal and non-fatal stroke compared to reference subjects sleeping 7–8 h per day [7].

Limitations of the study

One of the most significant limitations of our study is the absence of objective (instrumental) verification of sleep duration, although according to multiple studies self-reports correlate with the actigraphy data [26]. Another limiting factor is the cross-sectional design of our study. Short or long sleep duration is not always habitual. It might result from common sleep disorders (e.g., decrease in sleep time and low sleep quality in insomniacs, sleep apnea-related significant reduction in sleep quality). We also did not analyze the factors limiting sleep duration — the duration of work time, the time which subjects waste to get to the workplace, work schedule, chronotype and etc., because these factors were not included in the structured interview according to the primary design of the ESSE-RF study.

Conclusions

Our data support the concept of the relation between sleep and cardiometabolic disorders and provide additional evidence on the unfavorable impact of extreme sleep duration variations. We demonstrated that sleep duration is highly variable in Russian population with significant prevalence of short sleepers. However, unlike published data, in our cohort not all cardiovascular diseases were associated with sleep duration. The multivariable odds ratio was higher for obesity in short-sleepers compared with those who slept 7–8 hours. Meanwhile the U-shaped association was found for coronary artery disease. Association with myocardial infarction is characterized by the J-shaped relation. There were no associations for hypertension, diabetes mellitus and stroke. We believe that our results provide important information for the understanding of sleep epidemiology and relation between sleep and cardiovascular risk.

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Conflict of interest

None declared.

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