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Association between sleep duration and electrocardiographic ischemic changes in middle-aged population: Isfahan Healthy Heart Program

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Original Article

Abstract

BACKGROUND: Recent studies examining the association between sleep duration and cardiovascular disease (CVD) showed inconsistent results. The aim of our study was to evaluate the association between self-reported night sleep duration and ischemic changes in electrocardiography (ECG).

METHODS: We conducted this cross-sectional study on 3513 participants from Iranian middle-aged population as a part of Isfahan Healthy Heart Program (IHHP), Isfahan, Iran. Sleep duration was obtained by questioning participants. The frequency of electrocardiographic ischemic changes was calculated using ECG Minnesota coding system.

RESULTS: Short sleep duration was associated with increased frequency of electrocardiographic ischemic changes. In a fully adjusted multiple logistic regression analysis, the odds ratio (OR) for short sleep duration less than 5 hours per night was 1.501 [95% confidence interval (CI) for OR: 1.085-2.076] compared to 8 hours of sleep. After stratifying the study population into sex groups, the association remained significant only in women. The OR for short sleep less than 5 hours per night was 1.565 (95% CI for OR: 1.052-2.329) and 1.455 (95% CI for OR: 0.833-2.539) in women and men, respectively. There was no association between long sleep duration and electrocardiographic ischemic changes in men and women.

CONCLUSION: We concluded that there is a positive association between short sleep duration and frequency of electrocardiographic ischemic changes in middle-aged women. This association suggests that short sleep duration may increase the risk of ischemic heart disease (IHD) in women, and this need to be evaluated in further studies.

Keywords: Myocardial Ischemia, Electrocardiography, Sleep Deprivation

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Introduction

Ischemic heart disease (IHD) is the leading cause of death worldwide.[1] Recent studies suggest that sleep duration is related to cardiovascular mortality and morbidity.[2]

There are also many studies showing the association between sleep duration and cardiovascular risk factors such as diabetes, hypertension, obesity, and metabolic syndrome.[3-6] Prospective and cross-sectional studies which examined the association of sleep duration with cardiovascular disease (CVD) showed inconsistent results.

Some studies reported only short sleep duration, and some others reported long sleep duration as a risk factor for CVD.[7-10] Some other studies suggest a U-shaped association between short and long sleep duration with CVD;[11,12] moreover, there are some studies that claim no direct association between sleep duration and CVD, or suggest that the effect may be caused by other covariates.[13-15]

As we know, there is no study evaluating the relation between sleep duration and IHD in Iranian population. In this study we aimed to evaluate the association between habitual nocturnal sleep

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duration and frequency of ischemic changes in electrocardiography (ECG) in a middle-aged Iranian general population.

Materials and Methods

This cross sectional study was conducted as a part of Isfahan Healthy Heart Program (IHHP), Isfahan, Iran. Details of IHHP are published elsewhere.[16]

Individuals from urban and rural communities of three provincial cities of Isfahan, Najafabad, and Arak chosen by multistage cluster sampling were included. Inclusion criteria of our study were 35 to 60 years of age, Iranian nationality, history of residing in the above cities for at least 10 years, and absence of hemorrhagic disease and mental retardation. The study participants consisted of 3513 individuals based on inclusion and exclusion criteria.

Sociodemographic data were recorded by trained interviewers in door-to-door visits. Participants were asked to go to IHHP clinical centers and after signing informed written consent, medical history was taken and physical examinations were done for each individual. Fasting blood sugar (FBS) and lipid profile were measured by standard laboratory tests.

Twelve-lead ECG was taken by trained staff using Hewlett-Packard ECG machine from all participants. All the electrocardiograms were studied by the same cardiologists, and their corresponding codes were calculated. Ischemic changes were identified according to Minnesota coding system. We included four levels of ischemia in our outcomes: definite myocardial infarction (MI) which is defined by Minnesota codes 1.1, 1.2.1 and 1.2.2; possible MI represented by codes 1.2.7, 1.2.8, 1.3; definite ischemia equates codes 4.1 and 5.1; and possible ischemia which is diagnosed by codes 4.2, 5.2 and 5.3.[17]

Sleep duration time was obtained by the question "How many hours of sleep do you get per night usually?" Responses were categorized into 6 groups: less than 5 hours, 5 hours, 6 hours, 7 hours, 8 hours, and 9 hours and more.

Other covariates included in the analysis were: age by years, sex (men and women), body mass index (BMI) which was calculated as weight/height^2 (kg/m^2) and categorized into 30 ≤ and < 30 groups, physical activity measured by validated Baecke questionnaire of habitual physical activity and stratified into two groups of active and inactive, smoking status (never, past smoker, current smoker),[16,18] metabolic syndrome components defined as following: 1- central obesity as the waist circumference > 102 cm in men and >88 cm in women; 2- fasting plasma triglycerides ≥ 150; 3- low high-density lipoprotein (HDL) cholesterol with fasting HDL cholesterol < 40 mg/dl in men and < 50 mg/dl in women; 4- hypertension with systolic blood pressure ≥ 130 mmHg and/or diastolic blood pressure ≥ 85 mmHg and/or antihypertensive agents; 5- hyperglycemia with fasting plasma glucose ≥ 100 mg/dl and/or hypoglycemic medications.[19]

The variables were reported as number (percentage) or mean [± standard deviation (SD)] as appropriate. We compared the characteristics of participants in different sleep duration groups, and also in two groups of individuals with and without ischemic changes in ECG by using chi-square test for categorical variables and analysis of variance (ANOVA) for continuous variables.

We used multiple logistic regression analysis to assess the impact of sleep duration on frequency of ischemic changes in ECG "defined by Minnesota codes". Odds ratios (OR) with 95% confidence interval (CI) were calculated for sleep groups using 8 hours of night sleep as the reference category, and 3 models were used for analysis: in the first model, we calculated OR for each group of sleep without any adjustment; in the second model, results were adjusted for age and sex; and in the third model results were additionally adjusted for BMI, smoking status, physical activity (active or Inactive), and metabolic syndrome components (5 groups having 1, 2, 3, 4 or 5 of the components).[19] In a second analysis, we stratified the study population into sex groups and calculated the OR for men and women separately. We chose 8 hours as the reference group because it had the lowest frequency of ischemic changes between sleep groups in our study, and also it is recommended as the optimal sleep duration time for middle-aged adults.[20] Statistical analysis was performed using SPSS software (version 15, SPSS Inc., Chicago, IL, USA). The study was approved by Ethics Committee of Isfahan Cardiovascular Research Center.

Results

In total, 3513 individuals aged 35 to 60 years participated in the study. Mean age of study population was 44.8 ± 6.8 years, 52.6 percent were women, and significant differences in age and sex were seen between sleep groups. Frequency of electrocardiographic ischemic changes according to ECG Minnesota coding was 21.4 %, and average sleep duration was 6.85 ± 1.48 hours. Characteristics of each sleep group are showed in table 1.

Table 1. Study population characteristics by sleep duration.

Sleep duration (hour per night)	< 5 hours	5 hours	6 hours	7 hours	8 hours	9 hours<	P*
Characteristic							
Number of participants	249	319	763	807	1133	234	
ECG ischemic changes	72 (28.9)	65 (20.3)	158 (20.7)	174 (21.6)	229 (20.2)	53 (22.6)	0.035
Women	148 (59.4)	149 (46.7)	394 (51.6)	439 (54.4)	583 (51.5)	128 (54.7)	0.043
BMI ≥ 30	56 (23.6)	78 (26.2)	202 (27.6)	190 (24.1)	264 (23.7)	58 (25.1)	0.491
BMI < 30	181 (76.4)	220 (73.8)	530 (72.4)	599 (75.9)	849 (76.3)	173 (74.9)	
Current smoking	36 (14.5)	59 (18.5)	98 (12.9)	107 (13.3)	153 (13.5)	44 (18.8)	0.051
Physical activity (inactive)	143 (57.4)	197 (61.8)	447 (58.6)	468 (58.0)	643 (56.8)	131 (56.0)	0.695
Age (year)	47.4 ± 6.7	46.0 ± 6.8	45.1 ± 6.8	44.2 ± 6.8	44.3 ± 6.8	43.9 ± 7.0	< 0.001
BMI (kg/m^2)	27.3 ± 4.3	27.3 ± 4.4	27.5 ± 4.5	27.2 ± 4.4	27.0 ± 4.4	26.8 ± 4.6	0.151
Metabolic syndrome (number of components)							
0	26 (10.6)	43 (13.7)	113 (15.0)	137 (17.1)	193 (17.2)	34 (14.5)	0.058
1	72 (29.4)	93 (29.5)	188 (24.9)	190 (23.8)	266 (23.6)	55 (23.5)	
2	63 (25.7)	84 (26.7)	240 (31.8)	259 (32.4)	347 (30.8)	73 (31.2)	
3	52 (21.2)	57 (18.1)	149 (19.8)	142 (17.8)	226 (20.1)	50 (21.4)	
4	28 (11.4)	35 (11.1)	50 (6.6)	64 (8.0)	72 (7.3)	17 (7.3)	
5	4 (1.6)	3 (1.0)	14 (1.9)	7 (0.9)	11 (1.0)	5 (2.1)	

Data are given as n (%) or mean ± standard deviation (SD)
* P-value calculated using chi-square test or ANOVA as appropriate.
ECG: Electrocardiography; BMI: Body mass index

Table 2 presents the characteristics of the study participants in two groups of with and without ischemic changes in ECG. The group with ischemic changes in ECG were more likely to be older, women, inactive, to sleep less, to have higher BMI and higher prevalence of metabolic syndrome components, but were less likely to smoke.

Compared to those who sleep 8 hours per night, individuals with short sleep duration (less than 5 hours) had increases in the frequency of ischemic changes (Table 3). In model 1 for those who sleep less than 5 hours OR was 1.606 (95% CI: 1.178-2.189); in model 2 adjusted for age and sex, OR was 1.410 (95% CI: 1.025-1.940). After adjustment for additional covariates in model 3, the OR was 1.501 (95% CI: 1.085-2.076). In subgroup analysis the association remained significant in women but not in men, the OR for < 5 hours of sleep in women and men were 1.565 (95% CI: 1.052-2.329) and 1.455 (95% CI: 0.833-2.539), respectively. (Table 4).

Table 2. Comparing variables in groups with and without ischemic changes in electrocardiography (ECG)

Variable	With ischemic changes in ECG	Without ischemic changes in ECG	P*
Number of participants	752	2761	
Sleep duration (hour)	6.74 ± 1.49	6.87 ± 1.47	0.046
Age (year)	45.80 ± 6.80	44.50 ± 6.80	< 0.001
Women (%)	66.2	47.0	< 0.001
BMI ≥ 30 (%)	26.5	22.1	0.002
Current smoking (%)	9.9	13.8	0.001
Physical activity (inactive) (%)	63.0	58.3	0.004
Metabolic syndrome components (%)			
0	10.7	15.3	0.001
1	21.1	24.5	
2	29.1	29.6	
3	22.7	20.1	
4	13.6	8.6	
5	2.8	1.9	

Data are given as percent or mean ± standard deviation (SD)
* P-value calculated using chi-square test or ANOVA as appropriate
ECG: Electrocardiography; BMI: Body mass index

Table 3. Association between sleep duration and ischemic changes in electrocardiography (ECG)

Sleep duration (hour)	Persons at risk	Model 1* OR (95% CI)	Model 2** OR (95% CI)	Model 3§ OR (95% CI)
Less than 5	249	1.606 (1.178-2.189)	1.410 (1.025-1.940)	1.501 (1.085-2.076)
5	319	0.991 (0.727-1.351)	0.990 (0.721-1.359)	0.947 (0.681-1.316)
6	763	1.031 (0.821-1.294)	1.010 (0.801-1.273)	1.022 (0.808-1.294)
7	807	1.085 (0.869-1.355)	1.059 (0.845-1.328)	1.063 (0.846-1.336)
8£	1133	1	1	1
9 and more	234	1.156 (0.824-1.622)	1.136 (0.804-1.605)	1.136 (0.800-1.600)

* Analysis without adjustment for covariates; ** Analysis adjusted for age and sex; § Analysis adjusted for age, sex, body mass index (BMI) (< 30, 30 ≤), smoking (past, never, current), physical activity (inactive, active), metabolic syndrome (number of components)
£ Reference group; OR: Odds ratio; CI: Confidence interval

Discussion

In this study, we observed that short sleep duration of less than 5 hours per night compared to 8 hours of sleep was associated with increased frequency of electrocardiographic ischemic changes in Iranian middle-aged women but not in men. This association was independent of age, smoking, BMI, physical activity, and metabolic syndrome components. We did not find any association between long sleep duration and ischemic changes.

Association of short sleep duration with IHD was reported in previous studies in other countries.[2,8,21-24] Meisinger et al. examined association between sleep duration and incidence of MI in Monica Augsburg cohort study. They stratified the subjects in sex groups and after adjustment for possible confounders the hazard ratio (HR) of MI in women sleeping ≤ 5 hours was 2.98 (95% CI, 1.48-6.03) compared with women sleeping 8 hours; the corresponding HR in men was 1.13 (95% CI, 0.66-1.92); thus, a positive association between short sleep duration and incidence of MI among middle-aged women but not in men was observed.[8] Their results were similar to our findings. Aggarwal et al. in a cross sectional study from the National Health and Nutrition Examination Survey of noninstitutionalized United States (US) civilians found that there was significant increase in MI prevalence in those with less than 6 hours of sleep and increase in coronary artery disease (CAD) prevalence in those with more than 8 hours of sleep.[25] Cappuccio et al. reported in their meta-analysis that both short and long sleep duration was associated with coronary heart disease (CHD).[26]

The possible mechanisms of association between short sleep duration and CVD are largely described in previous studies. These mechanisms include changes in appetite regulating hormones which lead to increased calorie intake,[27,28] increased sympathetic system activity,[29,30] dysregulation of endocrine system causing impaired glucose tolerance and increased cortisol secretion.[31,32] Another possible mechanism is due to inflammation process which promotes atherosclerosis.[33,34]

Table 4. Association between sleep duration and ischemic changes in electrocardiography (ECG) by sex groups

Sex group	Sleep duration (hour)	Persons at risk	Model 1* OR (95% CI)	Model 3** OR (95% CI)
Women	Less than 5	148	1.550 (1.054-2.277)	1.565 (1.052-2.329)
	5	149	1.050 (0.699-1.577)	1.002 (0.657-1.529)
	6	394	1.108 (0.831-1.478)	1.097 (0.819-1.470)
	7	439	1.257 (0.955-1.655)	1.242 (0.939-1.642)
	8£	583	1	1
	9 and more	128	1.119 (0.730-1.717)	1.134 (0.737-1.743)
Men	Less than 5	101	1.494 (0.866-2.576)	1.455 (0.833-2.539)
	5	170	0.995 (0.607-1.630)	0.860 (0.509-1.456)
	6	369	0.905 (0.615-1.332)	0.898 (0.603-1.338)
	7	368	0.738 (0.492-1.108)	0.765 (0.507-1.154)
	8£	550	1	1
	9 and more	106	1.156 (0.653-2.047)	1.181 (0.662-2.108)

* Analysis without adjustment for covariates; ** Analysis adjusted for age, body mass index (BMI) (< 30, 30 ≤), smoking (past, never, current), physical activity (inactive, active), metabolic syndrome (number of components)
£ Reference group; OR: Odds ratio; CI: Confidence interval

Studies which reported the association between long sleep duration and CVD were unable to find any specific mechanism for explaining the association. One hypothesis is that long sleep duration correlates by other comorbidities and underlying health issues that may cofound with CVD.[35-37] As comorbidities are more prevalent in elderly individuals, the association of long sleep duration with CVD should mostly be observed in old population and this can explain the absence of this association in our study of middle-aged population.

The gender-specific association between short sleep duration and electrocardiographic ischemic changes that we found is in concordance with some previous studies; Ikehara et al. conducted a cohort study to observe the association between sleep duration and mortality from CVD and other causes in Japan; and they found that the association between short sleep duration and IHD was only significant in women.[38]Also in Monica Augsburg cohort study this association was significant only in women.[8] There is no accurate explanation for this gender discrepancy, some different mechanisms may play role in the effect of sleep on IHD in women; women have different sleep patterns and sleep disorders,[39,40] some CVD risk factors that may interact with the association between sleep and CVD have different significances in women;[41,42] there are reports that show an association between short sleep duration and hypertension only in women.[43-45] All of these differences may reinforce the impact of short sleep on IHD in women and these gender differences need to be evaluated in further studies.

Our study had some limitations; first of all, the cross sectional design of study makes us unable to observe the causality and direction of association between sleep duration and IHD. Another limitation that also has been addressed in many previous studies is the subjective evaluation of sleep duration which may not be very accurate but it is still useful and reliable according to some researches.[46-48] We did not evaluate other sleep parameters like sleep disturbances, difficulty falling sleep, and sleep quality which seem to be important in interpreting the effect of sleep on CVD.

In this study, we performed ECG in all participants, which led in finding even asymptomatic patients with ischemia, although ECG is not enough criteria for diagnosing IHD. We adjusted the analysis for common IHD risk factors. We did not have data of sleep apnea in our population, but we tried to modify its effect by adjusting the analysis for BMI groups of 30 ≤ and 30 >.

Conclusion

In conclusion, this cross-sectional study of Iranian middle-aged population showed that short sleep duration may increase the risk of IHD in women, and this should be evaluated in further prospective studies.

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Conflict of Interests

Authors have no conflict of interests.

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