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SCIENTIFIC INVESTIGATIONS

Insomnia in patients with coronary heart disease: prevalence and correlates

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Study Objectives: The aim of this study was to determine the prevalence of insomnia and its association with clinical and psychosocial factors in a large sample of outpatients with coronary heart disease.

Methods: The sample comprised 1,082 patients, mean age 62 years (21% female), who participated in the cross-sectional NORwegian CORonary Prevention Study. Patients who were hospitalized with myocardial infarction and/or a coronary revascularization procedure in 2011–2014 responded to a self-report questionnaire and participated in a clinical examination with blood samples 2–36 (mean, 16) months later. Insomnia was assessed using the Bergen Insomnia Scale, a questionnaire based on the criteria for the clinical diagnosis of insomnia as described in the *Diagnostic and Statistical Manual of Mental Disorders*, fourth version. We performed bivariate logistic regressions for crude analysis and backward stepwise logistic regressions for multiadjusted odds ratios (OR).

Results: In total, 488 patients (45%) reported insomnia, and 24% of these patients had used sleep medication in the previous week. Anxiety symptoms (OR: 5.61) were the strongest determinants of insomnia, followed by female sex (OR: 1.88), diabetes (OR: 1.83), eating fish fewer than three times a week (OR: 1.69), type D personality (OR: 1.69), and C-reactive protein ≥ 2 mg/L (OR:1.58), in multiadjusted analyses.

Conclusions: Insomnia was highly prevalent in coronary heart disease outpatients. Psychological factors, lifestyle factors, and subclinical inflammation were associated with insomnia. Our results emphasize the need to identify patients with insomnia and provide appropriate management of insomnia in outpatients with coronary heart disease.

Keywords: insomnia; secondary prevention; coronary heart disease; cardiovascular risk factors; anxiety; depression; type D personality

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BRIEF SUMMARY

Current Knowledge/Study Rationale: A better understanding of insomnia among coronary heart disease patients may identify potential high-risk groups for insomnia and may contribute to the development of effective interventions. This study was the first to investigate the prevalence of insomnia and its associations with clinical and psychosocial factors in a sample of coronary heart disease outpatients.

Study Impact: Insomnia was highly prevalent, reported by more than 4/10 coronary heart disease outpatients. Anxiety, female sex, diabetes, low intake of fish, type D personality, and inflammation were the strongest predictors of insomnia. Our results emphasize the importance of identifying insomnia in coronary heart disease patients and providing appropriate management.

INTRODUCTION

Recently, focus has increased on psychological factors—in particular, anxiety and depression— and their associations with poor treatment compliance and risk of death and cardiac events in coronary heart disease (CHD) patients.[1] Few studies, however, have focused on insomnia, a condition characterized by difficulty with sleep initiation, maintenance, waking up too early, or nonrestorative sleep, despite an adequate opportunity to sleep, coupled with daytime impairment.[2]

To date, most studies of sleep in CHD patients have focused on obstructive sleep apnea (OSA) owing to the known associations between sleep-disordered breathing and CV morbidity.[3] Whereas some studies have focused on sleep quality and patterns of sleep in CHD patients (eg, Madsen et al, 2019), we are aware of only two previous studies that have focused specifically on insomnia in CHD patients.[4,5] In these studies, insomnia was assessed using the Insomnia Sleep Index[4,5]; however, this scale is not based on any diagnostic criteria for insomnia. Nevertheless, high prevalence rates of moderate to severe insomnia of 36%–37% have been reported during hospitalization and 4–6 weeks after the acute cardiac event.[4,5] It is likely that CHD events, like acute coronary syndromes, result in acute disturbances in sleep that may gradually return to normal levels[3]; however, psychological distress may also persist or even increase over time after a cardiac event.[6,7] To our knowledge, no studies have been done on the prevalence of insomnia in CHD outpatients more than 6 months after an acute cardiac event. Therefore, more studies of insomnia are needed in CHD outpatients.[3] This is of particular relevance because sleep disturbances, including insomnia, have been associated with increased risk of mortality and recurrence of cardiac events after acute coronary syndromes.[8–12]

Coryell et al (2013)[4] found that insomnia in CHD patients was only independently associated with liver disease, whereas DaCosta et al (2017)[5] found age, taking prescribed sleep medication, and depression to be associated factors in multiadjusted analyses. Assessment of C-reactive protein (CRP) and distressed type (type D) personality was not included in these previous studies, even though

recent studies suggest associations between sleep problems and type D personality in cardiac patients.[13,14] Thus, the relationship between insomnia and potentially important clinical and psychological variables in CHD patients remains largely unknown. Of particular interest is the lack of knowledge regarding the association between insomnia and inflammation, which also plays a pivotal role in the pathophysiology of atherosclerosis and CHD.

Knowledge of the determinants of insomnia in CHD patients is important for the identification of potential insomnia high-risk groups to advance our current knowledge and understanding of a potential link between insomnia and poor cardiac prognosis. Furthermore, better understanding of the determinants of insomnia may enhance secondary prevention and form the basis for novel and effective interventions tailored to CHD patients. We therefore determined the prevalence of insomnia in a CHD population by applying the Bergen Insomnia Scale (BIS), which is based on the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM-IV) criteria.[15] We also explored the clinical and psychosocial factors associated with insomnia.

METHODS

Design and population

The present study is based on data from the NORwegian CORonary Prevention study. This cross-sectional study has a retrospective component. A comprehensive description of design, methods, and baseline characteristics has been published elsewhere.[16] The study was conducted at two general Norwegian hospitals (ie, Drammen and Vestfold) with a combined catchment area of 380,000 inhabitants, constituting 7.4% of the Norwegian population. The catchment area has a representative blend of sociodemographic and clinical factors, urban and rural districts, geography, economy, age, morbidity, and mortality.[16]

In brief, patients aged 18–80 years with a first or recurrent coronary event, which was defined as acute myocardial infarction and/or a revascularization procedure (coronary artery bypass grafting or percutaneous coronary intervention), were identified from hospital discharge lists in the period 2011–2014. In patients with recurrent coronary events, the index event was defined as the last event recorded before the time of study inclusion. Patients were excluded according to the following criteria: a diagnosis of type 2 myocardial infarction; inability to understand the Norwegian language; cognitive impairment, including living in nursing homes; psychosis; drug abuse; short life expectancy owing to terminal heart (New York Heart Association class 4); lung, liver, or kidney disease (stage 5); or malignant disease. In all, participants consented to participate in the study 2–36 months (median: 16) after the index event. The data collection was conducted in 2014–2015 and comprised a standardized clinical examination, collection of blood samples, and a comprehensive self-report questionnaire. Drammen Hospital analyzed blood samples from both hospitals to avoid between-hospital differences.

Ethics

All participants gave signed informed consent before study participation. The study was approved by The Regional Committee of Ethics in Medical Research (2013/1885).

Variables

The following demographic and clinical characteristics data were collected from hospital records at the time of study inclusion: age, sex, coronary index diagnosis, participation in cardiac rehabilitation, comorbidity,[17] and a diagnosis of diabetes.

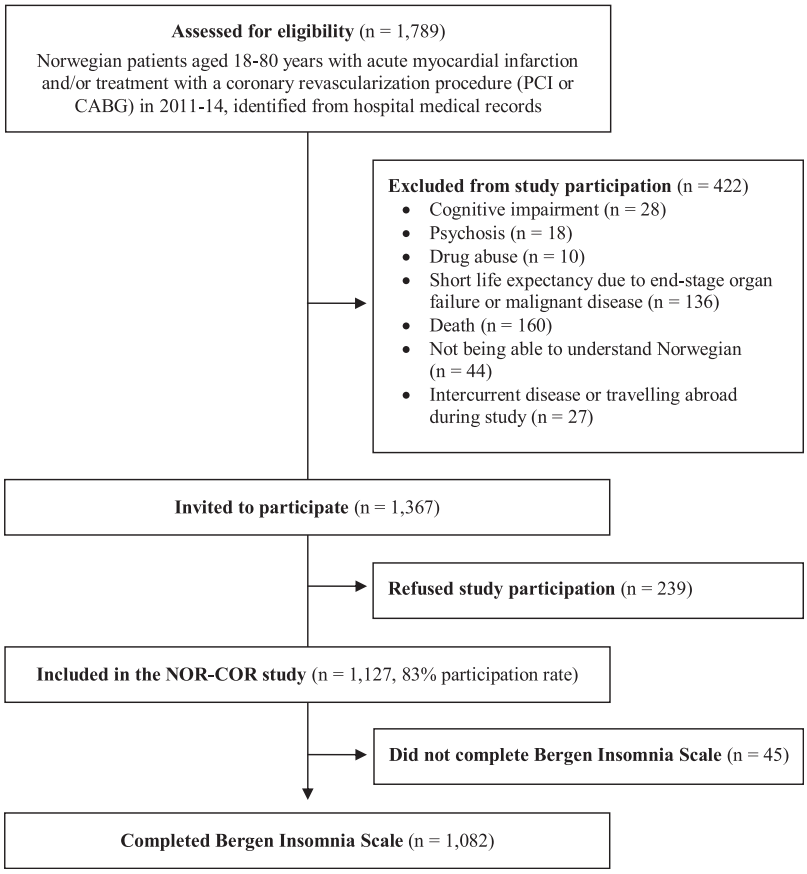
A comprehensive self-report questionnaire with good test-retest reliability[18] included assessments of the following: level of education (with *low education* defined as 12 years or less), living alone, *current* smoking (defined as daily smokers at time of study inclusion), physical activity (*physical inactivity* was defined as physical activity less than once a week), eating fish (*low intake* was defined as less than three times a week), risk of OSA (Berlin Questionnaire),[19] and taking sleep medication in the previous week (yes/no).

Insomnia was assessed by the BIS,[15] which is a six-item questionnaire based on the criteria for the clinical diagnosis of insomnia described in the *Diagnostic and Statistical Manual of Mental Disorders*, fourth version (DSM-IV-TR). The first four items inquire about difficulties with sleep initiation, maintenance of sleep, awakenings in the morning, and nonrestorative sleep; items five and six assess daytime impairment and satisfaction with sleep. A 30-minute cutoff value is used for the first three items. All items are scored as number of days per week (0–7), yielding a continuous sum score from 0 to 42 (BIS sum score), increasing with severity of insomnia symptoms. Contrary to the frequently used brief and psychometrically sound insomnia severity index,[20] the BIS comprises specific cutoff values for waking time (30 min) and number of days per week rather than unspecific response categories, which is more in accordance with the DSM criteria and normative data exists. The BIS can also be used as a diagnostic tool (insomnia vs no insomnia). Three days or more on items one, two, three, or four combined with 3 days or more on item five or six indicate a diagnosis of insomnia. Those who fulfilled these criteria were categorized with "insomnia", whereas those who did not fulfill these criteria were described as "no insomnia". The BIS has adequate psychometric properties, and there are normative Norwegian data for comparison.[15] In the present study, the 4-week test-retest reliability of the BIS was .92.[18]

Depression and anxiety were assessed using the Hospital Anxiety and Depression Scale (HADS).[21] This is a 14-item self-report questionnaire consisting of two seven-item subscales that assess anxiety (HADS-A) and depressive symptoms (HADS-D). A cutoff value of HADS-A or HADS-D ≥ 8 has been reported to represent clinically significant symptoms of anxiety or depression.[22] The HADS has demonstrated good psychometric properties in a number of studies, including in CHD patients.[22] The Norwegian version of the HADS has shown good internal consistency and acceptable validity across studies.[22]

The Type D Scale[23] was used for the assessment of type D personality. This scale consists of two seven-item subscales assessing negative affectivity (NA) and social inhibition (SI). Items are answered on five-point Likert scales ranging from 0 to 4. *Type D* is defined as having a score $\geq$ 10 on both the NA and SI subscales.[23] A Norwegian version was used that has been validated in a sample of CHD patients, with acceptable psychometric properties with Cronbach alphas of 0.87 for the NA

Figure 1—Study flow chart.



CABG = coronary artery bypass grafting, PCI = percutaneous coronary intervention.

subscale and 0.83 for the SI subscale[24] and with a test-retest reliability of 0.90 (NA subscale) and 0.91 (SI subscale) over a 1-month period.[18]

The clinical examination comprised the following: assessment of diastolic and systolic blood pressures with standardized procedures using a validated digital sphygmomanometer (Welch Allyn WA Connex ProBP 3400 Welch Allyn, Inc., Skaneateles Falls, New York), height (nearest 0.5 cm) and weight (nearest 0.5 kg), as well as blood sampling, including highly sensitive CRP and low-density lipoprotein cholesterol (both analyzed with Architect ci16200, Abbott Laboratories, Abbott Park, Illinois).

Statistics

Descriptive analyses were applied as frequencies (%) and means with standard deviations (SD). To test between-group differences, we performed chi-square tests to compare proportions and independent samples *t* test to assess between-group differences. To compare insomnia prevalence rates in various groups of time since index event, we performed chi-square test between four groups according to the time from the index event (0–6 months, > 6 months –12 months, > 12 months −24 months, and > 24 months). For crude odds ratios (OR), we performed bivariate logistic regressions and to derive trimmed models with multiadjusted OR, we used backward stepwise logistic regressions. All variables with bivariate *P* value (< .10) were retained in the backward stepwise procedure. Backward elimination was performed to hedge against possible statistical suppression. We also performed hierarchical analyses (stepwise forward regressions). Multicollinearity regarding study factors (clinical and psychological factors) was tested with standard variance inflation factors, and we found no indication of significant multicollinearity among the study factors. The questionnaire-based data had 0–10% missing values. To investigate the sensitivity of the backward regression model, we performed backward regressions, including OSA risk (**Table S1**) or participation in cardiac rehabilitation. In all bivariate and multivariate analyses, *P* values < .05 were considered statistically significant. The statistical analysis was performed using SPSS version 25 (IBM SPSS Statistics, Armonk, New York).

RESULTS

The study flow chart is shown in **Figure 1.** In short, 1,789 patients were identified from hospital discharge lists. Patients (n = 423) were excluded from study participation because of cognitive impairment (n = 28), psychosis (n = 18), drug abuse (n = 10), short life expectancy (n = 136), death (n = 160), inability to understand Norwegian (n = 44), and other (n = 27). Of 1,367 patients invited

to participate, 239 patients refused to participate (nonparticipants). BIS data were missing for 45 patients. Compared with participants, the nonparticipants were more likely to be women (28% vs 21%, $P < .05$). No significant difference in age was found between the groups. Compared with BIS responders, BIS nonresponders were older at the index event (mean years 66.0 vs 61.5, $P = .001$), but they did not differ significantly as to their sex **(Table S3** in the supplemental material).

The mean age was 62 (SD 10) years, and 21% were females. Myocardial infarction was the index event in 858 patients (79%); 224 patients (21%) had stable or unstable angina. The mean BIS sum score was 13.9 (SD 10.8), and 488 patients (45%) fulfilled the BIS criteria for insomnia. Fifty-eight percent (130/226) of the females and 42% (358/856) of the males fulfilled the BIS insomnia criteria.

Table 1 shows the sociodemographic, clinical, and psychosocial characteristics among patients with and without insomnia. Younger age, female sex, education 12 years or less, and living alone were all significantly associated with insomnia. Among clinical factors, CRP ≥ 2 mg/L, current smoking, diabetes, physical inactivity, body mass index > 30 kg/m^2, eating fish less than three times a week, and OSA were also associated with insomnia. In all, 24% of those with insomnia reported using sleep medication, with a mean of 5.8 (SD 2.4) days in the previous week. Seven percent of patients without a diagnosis of insomnia used sleep medication in the previous week.

The levels and prevalence rates of clinically significant anxiety and depression symptoms were significantly higher among patients with insomnia compared with those without insomnia Furthermore, type D personality was significantly more prevalent among patients with insomnia than among those without (28.2% vs 10.4%, $P < 0.001$).

The results from bivariate logistic regression analyses are presented in **Table 2**. **Table 3** presents the final results from the backward elimination logistic regression analyses, in which eligible variables (ie, the sociodemographic, clinical, and psychosocial factors listed in **Table 2**) with P values < 0.10 were retained at each step. In the final multivariate model, anxiety (HADS-Anxiety ≥ 8) was the strongest determinant of insomnia in line with what was found in the bivariate analysis. Furthermore, diabetes, eating fish < 3 times a week, and CRP ≥ 2 mg/L remained significant after multiadjustment. The strength of association between insomnia and type D personality decreased but remained significant, whereas depression (HADS Depression ≥ 8) as well as age, physical activity < 1 times per week, current smoking, and body mass index > 30 kg/m^2 were no longer associated with insomnia. Hierarchical analyses (stepwise forward regressions) hardly changed the ORs for individual independent variables **(Table S2).**

Ancillary analyses also showed that anxiety symptoms statistically interacted with type D personality, with stronger effects of anxiety among those without type D personality ($P = .001$) and with depression symptoms, with stronger effects of anxiety symptoms among those with low levels of depression symptoms ($P = .018$). Prevalence of insomnia was not significantly different between the time groups since the index event (0–6, 6–12, 12–24, and > 24 months), not shown **(Table S4** and **Table S5).** The Cronbach alphas in our study were 0.88 for BIS sum score, 0.84 for HADS-A, 0.76 for HADS-D, and 0.89 for Type D Scale.

Finally, we also performed hierarchical analyses (stepwise forward regressions) with the intention of identifying the separate contributions of clinical, inflammatory, and psychological factors of insomnia; however, stepwise forward regressions hardly changed the ORs for individual independent variables **(Table S2).**

DISCUSSION

Forty-five percent of this representative outpatient sample with CHD fulfilled the criteria of insomnia according to the BIS, and three of four patients with insomnia did not report any use of sleep medication. Anxiety was the major potentially modifiable factor most strongly associated with insomnia. Moreover, diabetes, low fish intake, type D personality, and subclinical inflammation were other factors associated with insomnia.

The proportion of patients who met the criteria for insomnia (45%) is slightly higher than that (36%–37%) shown in previous studies of CHD patients.[4,5] This difference may be explained by the use of different questionnaires to assess insomnia; however, the prevalence rate in our study is also higher than that found in population-based studies, including a recent Norwegian study (20%) that also used the BIS.[25] Moreover, the mean BIS score in our study is higher than the published normative data from a Norwegian community sample (13.9 vs 10.7, $P < .001$).[15]

A decline in the prevalence of insomnia with increasing time since a cardiac index event has been previously hypothesized.[3] We found, however, no differences in the prevalence rates of insomnia with increasing time since the coronary event (range: 2–36 months). This is relevant because it has been suggested that an acute coronary event may result in concomitant sleep disturbances such as insomnia, which would, presumably, gradually return to normal levels over time; however, our results seem to indicate a high prevalence of insomnia also in the long term (mean: 16 months) after the cardiac event. Thus, insomnia is a prevalent condition that should be attended to in CHD outpatients.

The BIS was developed in accordance with the DSM-IV criteria for insomnia[15]; however, we also estimated the prevalence of insomnia according to the recent DSM-V criteria for insomnia by omitting the nonrestorative sleep criterion. This analysis revealed that the prevalence rate was reduced from 45.1% to 40.5%. Thus, 89.8% of the patients that fulfilled DSM-IV criteria also fulfilled DSM-V criteria, which is in line with results of a recent study.[25]

Disturbed sleep, including insomnia, was strongly associated with being a female, and this is in line with results from previous studies on CHD patients.[26–28] It is particularly noteworthy that almost six of 10 females reported insomnia. Interestingly the very pronounced bivariate sex difference (more insomnia among females) could not be explained or indeed reduced by putative intervening or mediating variables like personality and/or anxiety/depression. In our study, living alone was associated with insomnia, in line with data from a Japanese study.[28] Younger age was also associated with insomnia, which is consistent with the results of one previous study,[5] but it is not consistent with the results of the study by Coryell et al (2013).[4] In contrast to our results, lower education has not previously been significantly associated with insomnia in CHD patients, which may be due to lack of statistical power in previous studies because of few participants.[4,5]

Table 1—Characteristics in coronary patients with and without insomnia.

	Insomnia (n = 488, 45.1%)	No Insomnia (n = 594, 54.9%)	*P* Value**
Sociodemographic factors			
Age (y), mean (SD)	60.2 (9.9)	62.5 (9.3)	<.001
Female, n (%)	130 (26.6)	96 (16.2)	<.001
Months between index event and follow-up, mean (SD)	16.7 (10.4)	17.3 (10.6)	.286
Low education (≤ 12 years), n (%)	354 (73.8)	396 (66.9)	.015
Living alone, n (%)	104 (23.2)	90 (16.2)	.005
Clinical factors			
Coronary index diagnosis			
Acute myocardial infarction, n (%)	390 (79.9)	468 (78.8)	.648
Stable or unstable angina, n (%)	98 (20.1)	126 (21.2)	
> 1 coronary event before index event, n (%)	150 (30.7)	175 (29.5)	.649
Participation in cardiac rehabilitation, n (%)	231 (47.3)	316 (53.2)	.055
CRP ≥ 2 mg/L, n (%)*	214 (46.6)	196 (34.9)	<.001
Charlson comorbidity score, mean (SD)	4.0 (1.4)	4.1 (1.4)	.285
Coronary risk factors at interview			
Low-density lipoprotein cholesterol > 1.8 mmol/L, n (%)	280 (58.9)	322 (55.6)	.276
Currently smoking, n (%)	114 (23.9)	105 (18.6)	.033
Diabetes, n (%)	102 (20.9)	81 (13.6)	.002
Physical activity < 1 times per week, n (%)	104 (21.8)	80 (13.8)	.001
Blood pressure > 140/90 (140/80 diabetes) mmHg, n (%)	190 (42.8)	250 (46.7)	.218
Body mass index > 30 kg/m^2, n (%)	165 (37.1)	160 (29.9)	.018
Medication at interview			
Antithrombotic, n (%)	13 (2.7)	12 (2.0)	.483
Statins, n (%)	39 (8.0)	35 (5.9)	.173
Beta-blockers, n (%)	372 (76.2)	419 (70.5)	.036
Dietary factors			
Eating fish < 3 times/wk, n (%)	250 (51.2)	252 (42.4)	.004
OSA risk (yes/no), n (%)	243 (58.4)	187 (37.3)	<.001
Taking sleep medication past wk, n (%)	115 (23.8)	44 (7.6)	<.001
No. of days/w taking sleep medication, mean (SD)	5.8 (2.4)	5.5 (2.6)	.448
Psychosocial factors			
Bergen Insomnia Scale sum, mean (SD)	23.3 (8.6)	6.4 (4.9)	<.001
HADS-A sum score, mean (SD)	6.4 (4.0)	3.5 (2.9)	<.001
HADS-D sum score, mean (SD)	5.1 (3.5)	2.9 (2.6)	<.001
HADS-A ≥ 8, n (%)	170 (36.5)	51 (8.8)	<.001
HADS-D ≥ 8, n (%)	113 (23.9)	43 (7.3)	<.001
Type D personality, n (%)	135 (28.2)	61 (10.4)	<.001

*Excluded cases > 15 mg/L. ***P* calculated with *t* test for mean and chi-square for n. CRP = C-reactive protein, HADS-A = hospital anxiety and depression rating scale- anxiety subscale, HADS-D = hospital anxiety and depression rating scale- depression subscale, OSA = obstructive sleep apnea, SD = standard deviation, Type D = distressed type.

Disturbed sleep (including sleep disorders) was associated with poor immune functioning and inflammation in a recent meta-analysis and review based on population studies.[29] An association between insomnia and CRP, a marker of subclinical inflammation, has previously also been reported in a population-based study[30] and in CV patients[28] but these associations disappeared after adjustment for relevant confounders. In our study, insomnia was associated with CRP, also in multiadjusted analyses. A possible explanation for the contradictory results may be differences in the assessment methods for insomnia. Suggested mechanisms for this association are that insomnia may activate the hypothalamus-pituitary-adrenal axis and the sympathetic nervous system and thus may lead to a proinflammatory response.[31] The possible associations between insomnia and CRP in CHD patients are important because

Table 2—Odds ratios for insomnia by sociodemographic, clinical and psychosocial factors.

	Odds Ratio*	95% CI	*P* Value
Sociodemographic factors			
Age per 1 yr	.98	0.96–0.99	<.001
Female	1.88	1.40–2.53	<.001
Low education	1.39	1.07–1.81	.015
Living alone	1.56	1.14–2.14	.006
Clinical factors			
CRP ≥ 2 mmol/L	1.63	1.27–2.10	<.001
Low-density lipoprotein cholesterol, per 1 mmol/L	1.15	0.98–1.35	.087
Current smoking	1.38	1.03–1.86	.034
Diabetes	1.67	1.22–2.31	.002
Physical activity < 1 times per wk	1.74	1.26–2.40	.001
Body mass index > 30 kg/m^2	1.38	1.06–1.80	.018
Eating fish < 3 times/wk	1.43	1.12–1.81	.004
Psychosocial factors			
HADS A ≥ 8	5.95	4.22–8.39	<.001
HADS D ≥ 8	3.96	2.72–5.77	<.001
Type D personality	3.38	2.42–4.71	<.001

*Calculated from bivariate logistic regression analyses. CRP = C-reactive protein, HADS-A = hospital anxiety and depression rating scale- anxiety subscale, HADS-D = hospital anxiety and depression rating scale- depression subscale, Type D = distressed type.

Table 3—Multiadjusted odds ratios for insomnia.

	Odds Ratio*	95% CI	*P* Value
Sociodemographic factors			
Age per 1 yr	.98	.97–1.00	.087
Female	1.88	1.25–2.83	.002
Clinical factors			
CRP ≥ 2 mmol/L	1.58	1.13–2.22	.008
Diabetes	1.83	1.17–2.87	.009
Physical activity < 1 times per week	1.47	.93–2.31	.100
Eating fish < 3 times/wk	1.69	1.21–2.36	.002
Psychosocial factors			
HADS A ≥ 8	5.61	3.37–9.35	<.001
HADS D ≥ 8	1.76	.99–3.13	.054
Type D personality	1.69	1.02–2.81	.043

*Adjusted for all variable with $P \leq .10$ retained in backward elimination logistic regression analysis, likelihood ratio method. CRP = C-reactive protein, HADS-A = hospital anxiety and depression rating scale- anxiety subscale, HADS-D = hospital anxiety and depression rating scale- depression subscale, Type D = distressed type.

low-grade inflammation seems to promote insulin resistance, atherosclerosis, endothelial dysfunction, and plaque rupture, thus possibly representing a biological mechanism linking insomnia to poor CV prognosis, which should be addressed in future longitudinal studies.

In our study, obesity, diabetes, and physical inactivity were all associated with insomnia, but only diabetes remained significant in adjusted analyses. Sleep plays an important role in regulating metabolic functions and glucose homeostasis,[32] and insomnia has been observed in 47% of patients with diabetes.[32] Untreated, insomnia results in fluctuating glycemic levels and has been associated with poor glycemic control in patients with diabetes.[32] Sleep is associated in modulating insulin production, insulin sensitivity, glucose use, and glucose tolerance through the night. Inadequate sleep activates the sympathetic nervous system, and overactivity of the sympathetic nervous system may lead to insulin resistance. Furthermore, chronic or partial sleep loss can increase low-grade inflammation, contributing to increased insulin resistance and diabetes.[32] Thus, insomnia treatment may be particularly important in CHD patients with diabetes.

Eating fish less than three times a week was a risk factor strongly associated with insomnia in the adjusted analysis. More than half of those with insomnia reported low fish intake. There are some indications from population studies that a higher intake of fish is associated with better sleep quality as well as with sleep duration in men.[33] Hence, our results are consistent with these findings. Fatty fish is a source of long-chain omega 3 polyunsaturated fatty acids (omega-3) and vitamin D, both of which have a positive correlation with sleep quality.[34] Serotonin is involved in sleep regulation, and omega-3 plays an important role in the secretion of serotonin[33]; however, we did not particularly assess fatty fish intake, and our report of fish intake may represent a regional effect, and previous studies have not specifically reported the associations between insomnia and fish intake in CHD patients. Hence, this relationship should be further explored in future studies.

The co-occurrence of insomnia with anxiety and depression is well known, but the assessments of such associations are sparse in CHD patients.[3] Our results of insomnia being associated with anxiety and depression have only been reported in a previous small study of CHD patients.[4] Noteworthy, about three of four patients with insomnia reported at least moderate depressive symptoms in the study by Coryell et al,[4] whereas in our study only 24% of the patients with insomnia reported depression. Whereas the previous study indicated that screening for depression may help identify those with insomnia, our own study found anxiety to be more closely associated with insomnia than depression. Indeed, 37% among those with insomnia also reported clinically significant anxiety symptoms. The relationship between insomnia and anxiety has been somewhat less studied than that of depression, but our results are in line with the results of population studies that have shown that anxiety disorders as a cluster are the most common group of disorders in persons with insomnia.[35] Most patients with insomnia, however, did not report significant anxiety or depression symptoms in our study.

We identified an interaction between anxiety and depression. Patients who reported subclinical symptoms of anxiety as well as clinical symptoms of depression were more likely to report insomnia. The overall associations between insomnia, anxiety, and depressive symptoms in CHD patients are consistent with previous relevant studies, but to our knowledge, statistical interactions between these constructs have not yet been reported in CHD patients.

The extent to which anxiety or depression shows the strongest association with sleep disturbance, including insomnia, has varied.[4,5,27,28] The exact nature of this association is difficult to determine, but a bidirectional relationship is indeed likely to exist between insomnia and depression according to a recent review.[3] One study reported symptoms of anxiety and depression at 12 months being associated with sleep disturbances assessed at 4 months, but not at 6 weeks after a cardiac event.[36] A Norwegian population study reported insomnia to be a predictor of anxiety and depressive symptoms (HADS) 11 years later, even after adjusting for potential confounders.[37] Moreover, a recent study identified mechanisms to suggest that even modest improvements in sleep may reduce anxiety.[38] Whether insomnia coexists as a precursor, a residual symptom, or a core symptom of anxiety and depression needs further study. Thus, prospective cohort studies of insomnia, anxiety, and depression in CHD patients have been requested.[3]

In our study, type D personality was associated with insomnia in multiadjusted analyses, after adjusting for anxiety and depression. Hence, the association between type D and insomnia was not fully mediated by symptoms of anxiety and depression, in contrast to what has previously been reported in CHD patients.[13] Interestingly, we found an interaction between anxiety and type D personality. Patients with subclinical symptoms of anxiety were more likely to have insomnia if they had a type D personality. In contrast, those with clinical symptoms of anxiety did not change their probability of having insomnia with personality D being present. Type D, as well as insomnia, anxiety, and depression have previously been proposed as possible risk factors for poor prognosis in CHD patients, but a better understanding of the relative importance of these factors and potential prognostic pathways is needed.[39]

Our results suggest that inactive adults, current smokers, and those with body mass index ≥ 30 are at higher risk for incident insomnia, emphasizing the potential importance of promoting a healthy lifestyle with strategies such as encouraging smoking cessation, weight reduction, and physical activity that may alleviate insomnia among some CHD patients. In our study, the insomnia patients that reported use of sleep medication (24%) reported significantly higher symptom scores of anxiety and depression compared with those who reported no use of sleep medication. Similar relationships were found among those without insomnia. Our results suggest that in both those with and without insomnia, the reported use of sleep medication may be a marker for high psychological distress. In addition to sleep medication, cognitive behavioral therapy for insomnia (CBT-I) is regarded as the treatment of choice for insomnia[40]; however, this was not assessed in our study.

Limitations

This study has certain limitations. First, self-reported data are vulnerable to biases and may yield different results from those of a diagnostic interview. Therefore, prevalence should be interpreted as positive screening based on self-reported data. Moreover, even though BIS has been validated in previous studies, it has not been validated in CHD patients. Yet, a good test-retest reliability is reported for all key questionnaires in our study, including BIS, HADS, and Type D Scale.[18] Second, even though comprehensive data collection from questionnaires, clinical examination, and hospital records reduces the risk of unmeasured confounders, undetected confounders can never be excluded. Third, the Berlin questionnaire rather than polysomnography was applied for the assessment of OSA. No objective measure of sleep (eg, actigraphy) was applied, and we did not assess duration of sleep or use of treatment other than medication (ie CBT-I, sleep hygiene, and relaxation techniques). Nonparticipants were more likely to be female, and because insomnia was associated with being female, our prevalence estimate of insomnia may be conservative. BIS noncompleters were few, and even though associated with higher age, we conclude that this difference may not significantly affect the insomnia prevalence estimate. In addition, our study is cross-sectional, which reduces the possibilities of causal interpretations. A high participation rate (83%), recruitment of patients from routine clinical practice, and a comprehensive data set are among the strengths of the study.

CONCLUSIONS

Insomnia was highly prevalent in CHD outpatients and associated with psychological factors, lifestyle factors, and subclinical inflammation. Our results emphasize the importance of identifying patients with insomnia and provide appropriate management of insomnia. Because insomnia was associated with several CV risk factors, future studies of insomnia and CV prognosis in CHD patients are recommended.

ABBREVIATIONS

BIS, Bergen insomnia scale
CHD, coronary heart disease
CRP, C-reactive protein
CV, cardiovascular
DSM, Diagnostic and Statistical Manual of Mental Disorders
HADS, hospital anxiety and depression rating scale
HADS-A, hospital anxiety and depression rating scale-anxiety subscale
HADS-D, hospital anxiety and depression rating scale-depression subscale
NA, negative affectivity
OR, odds ratio
OSA, obstructive sleep apnea
SD, standard deviation
SI, social inhibition
Type D, distressed type

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