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Original Study

Relationship Between Nutritional Status and Insomnia Severity in Older Adults

Pinar Soysal MD [a,*], Lee Smith PhD [b], Ozge Dokuzlar MD [c], Ahmet Turan Isik MD [c]

[a] Department of Geriatric Medicine, Bezmialem Vakif University, Faculty of Medicine, Istanbul, Turkey
[b] The Cambridge Centre for Sport and Exercise Sciences, Anglia Ruskin University, Cambridge, United Kingdom
[c] Department of Geriatric Medicine, Faculty of Medicine, Dokuz Eylul University, Izmir, Turkey

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A B S T R A C T

Objectives: Both insomnia and malnutrition are quite common and can cause similar negative consequences, such as falls, depression, and cognitive impairment in older adults, but there is no study investigating the relationship between the 2. The aims were to investigate relationships between insomnia/insomnia severity and Mini Nutritional Assessment (MNA) score and serum nutrient levels.
Setting and participants: Aged 65 years or older, 575 outpatients were included.
Methods: MNA scores >23.5, 17-23.5, and <17 were categorized as normal nutritional status, malnutrition risk, and malnutrition, respectively. Serum vitamin B_{12}, vitamin D, and folate deficiencies were also evaluated. Insomnia Severity Index (ISI) with scores of 8 and higher indicated insomnia, which was further stratified as mild (8-14), moderate (15-21), or severe (22-28).
Results: The mean age was 73.1 ± 7.7 years, with 73.2% being female. The prevalence of patients with no insomnia, mild insomnia, moderate insomnia, and severe insomnia were 34.4%, 20.9%, 30.1%, and 14.6%, respectively. After adjusting for gender, education, number of drugs, Charlson Comorbidity Index, presence of depression, and Mini-Mental State Examination scores, patients with insomnia had lower MNA scores than those without insomnia (OR = 0.84, 95% CI: 0.7-0.9, $P < .001$). There were significant relationships between moderate/severe insomnia and the presence of malnutrition and risk of malnutrition (OR = 1.6, 95% CI: 1.0-2.5, $P = .046$; OR = 1.6, 95% CI: 1.0-2.7, $P = .042$) and MNA scores (OR = 0.83, 95% CI: 0.7-0.9, $P < .001$)/OR = 0.82, 95% CI: 0.7-0.9, $P < .001$). There was no significant difference between insomnia severity status and serum vitamin D, vitamin B_{12}, folate levels, or classification of these nutrients ($P > .05$).
Conclusions/Implications: There is a close relationship between MNA scores and insomnia or insomnia severity in older adults. Therefore, when evaluating an older patient with insomnia, malnutrition should be evaluated, or insomnia should also be questioned in an older patient with malnutrition. Thus, more effective management of the 2 can be possible.
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Insomnia is defined as persistently having difficulty in initiating and sustaining sleep, or waking up too early in the mornings and not falling asleep again.[1] Although the prevalence of insomnia is 12% to 20% in the general population, it ranges from 30% to 48% in older adults.[2] In a study of 6899 older adults aged 65 years and older, the incidence of annual insomnia was found to be 7%, and it has been reported that some drugs (eg, beta blockers) and comorbidities such as chronic pain, depression, cancer, chronic obstructive pulmonary disease, cardiovascular diseases, and some other factors, such as inactivity and decreased social relationships and caregiving, are increasingly associated with insomnia.[3] On the other hand, regardless of all these and similar factors, aging-related circadian rhythm disturbances can contribute to the development of later-life insomnia, such as changes in the amplitude of the circadian oscillation of physiological parameters like melatonin or the decrease in the effectiveness of the suprachiasmatic nucleus in the hypothalamus.[4] If not treated, insomnia can lead to dementia, depression, anxiety, delirium, diminished quality of life, falls, and cardiovascular diseases such as hypertension, myocardial infarction, and stroke.[4,5] With the appropriate treatment of insomnia, the development of such complications can be prevented. However, as well as insomnia, drugs used to treat it have a number of side effects.[6] For this reason, the number of studies investigating the reversible causes of insomnia in recent years has increased.

* Address correspondence to Pinar Soysal, MD, Department of Geriatric Medicine, Bezmialem Vakif University, Faculty of Medicine, Adnan Menderes Bulvarı (Vatan Street), 34093 Fatih, İstanbul, Turkey.
E-mail address: dr.pinarsoysal@hotmail.com (P. Soysal).

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Both micronutrient deficiencies and malnutrition or malnutrition risk are quite common and are risk factors for a variety of negative consequences, such as sarcopenia, frailty, falls, depression, and cognitive impairment in older adults.[7–9] In only a few of these studies, however, was a significant relationship shown between micronutrient abnormalities and sleep following the evaluation of the effect of nutritional factors on insomnia.[10–12] One study found a relationship between low serum vitamin D levels and short sleep duration and lower sleep efficiency in older men.[11] Another identified a correlation between vitamin B_{12}, vitamin D, and folate deficiency and sleep disturbance.[8] Moreover, although malnutrition is as important as micronutrient deficiency and is common, to our knowledge, there is no study investigating the relationship between malnutrition and insomnia.

Therefore, the aim of this study was to investigate the relationship between Mini Nutritional Assessment scores/nutrients and insomnia or insomnia severity in older adults.

Methods

Patients

A total of 575 older outpatients who were admitted to a geriatric clinic were included in this study. All the patients underwent comprehensive geriatric assessment.[13] The investigation conformed to the Declaration of Helsinki and was approved by our local ethics committee. Informed consent was provided by each participant or a legal guardian before participating in the study.

Patients who had severe illness that may impair their general health status, such as acute cerebrovascular event, sepsis, acute renal failure, acute coronary syndrome, and acute respiratory failure; patients younger than 65 years; patients who did not agree to undergo the comprehensive geriatric assessment; and patients who take medication for sleep disorders or who take nutritional supplements for malnutrition or nutrient deficiencies were excluded. Patients with moderate and severe dementia were also ruled out because self-reports based on their memory might be unreliable for questions about insomnia and nutrition, but patients with mild dementia were included.

Patients' Characteristics

Patients' age, gender, education level, and drugs were recorded. Those with hypertension, ischemic heart disease, congestive heart failure, diabetes mellitus, peripheral arterial disease, chronic obstructive pulmonary disease, cerebrovascular disease, or Parkinson's disease were identified by their or caregivers' self-reports. In addition, comorbidity status of the patients was evaluated using the Charlson Comorbidity Index.[14] Dementia and depression were diagnosed according to *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5), criteria.[15] All the participants underwent the Mini-Mental State Examination, and Geriatric Depression Scale-15 for neurocognitive evaluation.[16,17]

Nutritional Evaluation

Mini Nutritional Assessment (MNA) was performed in all patients to detect nutritional status, even if their MNA-Short Form scores were $\geq$12. If the total score was >23.5, 17-23.5, or <17, it was accepted as well-nourished, risk of malnutrition, or malnutrition, respectively. The MNA test is composed of simple measurements and 18 brief questions that can be completed in <10 minutes: anthropometric measurements (4 questions related to body mass index, weight loss, brachial circumference, and calf circumference); global assessment (6 questions related to lifestyle, medication, and mobility); and dietary questionnaire and subjective assessment (8 questions related to number of meals, food and fluid intake, autonomy of feeding, and self-perception of health and nutrition).[18] Because of the potentially multifactorial origin of nutritional risk in the older adults, the MNA was specifically designed and validated for older adults. Given its multidimensional approach, the MNA properly addresses this requirement, and the prevalence of nutritional conditions provided by the MNA appears in the measure able to reflect the nutritional features.[19] To calculate body mass index, height was measured to the nearest centimeter and weight was measured to the nearest half-kilogram with the same stadiometer.

Assessment of Insomnia

The Insomnia Severity Index (ISI) consists of 7 questionnaire items that capture self-reported symptoms and daytime consequences of insomnia, according to criteria from the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*. ISI scores range from 0 to 28, with higher scores indicating more severe insomnia. ISI scores of 8 or higher indicated insomnia, with severity further stratified according to ISI score as subthreshold (herein termed mild) (8–14), moderate (15–21), and severe (22–28).[20,21]

Vitamin B_{12}, Folate, and Vitamin D Assessment

To evaluate the biochemical evidence of insufficient intake and the metabolic condition, blood samples were collected in the morning after at least 8 hours of fasting. Serum vitamin B_{12} level was considered to be deficient and low when it was <200 pg/mL and <400 pg/mL, respectively.[22] Vitamin B_{12} was also evaluated according to a cut-off of 150 pg/mL.[23] Folate deficiency and low folate levels were evaluated according to both <3 ng/mL and <6 ng/mL, respectively.[7] After blood sample collection, the gel tubes were centrifuged within 1 hour and the sera stored at −20°C for serum vitamin D analysis. 25(OH)D was measured using a radioimmunoassay method. Patients with 25(OH)D < 10 ng/mL were considered to have vitamin D deficiency, and 25(OH)D of 10 to 20 ng/mL was accepted as insufficiency.[24]

Laboratory Findings

Laboratory tests were performed to assess the biochemical, metabolic, and nutritional status of the patients, including measurements of complete blood count, kidney and liver functions, cholesterol levels, thyroid-stimulating hormone, and HbA1c. All these biochemical tests were performed using the Diagnostic Modular Systems auto analyser (Roche E170 and P-800).

Statistical Analyses

Data were analyzed using SPSS, version 22. Descriptive statistics are shown as mean ± standard deviation for variables with normal distribution, median (minimum to maximum) for non-normal distributions, and number of cases and percentage for nominal variables. When the group number was 2, the significance of differences between the groups in terms of averages was investigated by *t* test, and if in median values, it was investigated by Mann-Whitney test. When the number of groups was more than 2, the significance was investigated by analysis of variance and the Kruskal-Wallis test for averages and medians, respectively. Nominal variables were assessed by the Pearson chi-square or Fisher exact test. Variances in more than 2 groups were assessed by post hoc Tukey tests. We used linear regression and logistic regression to analyze associations between sleep status and nutritional status and MNA scores, adjusting for all covariates including gender, education, number of drugs, Charlson Comorbidity Index, presence of depression, and Mini-Mental State

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Examination scores. For $P < .05$, the results were considered statistically significant.

Results

The mean age of the 575 patients in the sample was 73.1 ± 7.7 (73.2% of them female), and the mean education level was 3.2 ± 1.9. The prevalence of patients without insomnia (ISI < 8) was 34.4%. The prevalence of patients with mild insomnia, moderate insomnia, and severe insomnia was 20.9%, 30.1%, and 14.6%, respectively. There is no difference between the groups in terms of laboratory findings, including kidney and liver functions, cholesterol levels, and thyroid-stimulating hormone ($P > .05$). Table 1 shows demographic and clinical characteristics. There was a significant difference between groups in terms of gender, education, number of drugs, Charlson Comorbidity Index, presence of depression, and Mini-Mental State Examination scores ($P < .05$). The 4 insomnia severity groups were compared with respect to nutritional parameters, and lower MNA scores and higher rates of malnutrition and malnutrition risk were detected in patients with moderate and severe insomnia compared to the patients with mild insomnia or without insomnia ($P < .001$). When groups were adjusted for all covariates, the significant differences between nutritional status and insomnia severity status persisted ($P < .05$). There were no significant differences between insomnia severity status and serum vitamin D, Vitamin B_{12}, folate levels, or classification of these nutrients ($P > .05$).

The relations between nutritional status and insomnia groups were investigated using logistic regression analysis adjusting for all the covariates. Results showed that there was a statistically significant relationship between insomnia status and MNA and nutritional status ($P < .05$). Their odd ratios were shown in Table 2. Relationships between insomnia status and MNA and nutritional status were investigated using multiple linear regression models and are shown in Table 2. There were significant positive correlations between malnutrition/risk of malnutrition and insomnia/moderate and insomnia/severe insomnia, whereas insomnia status and MNA scores showed a significant negative correlation ($P < .05$).

Figure 1 shows the comparison of prevalence of insomnia according to nutritional status ($P < .05$).

Discussion

In this study, the relationship between insomnia and insomnia severity and nutritional status was investigated in the older adult, and MNA scores were found to be lower in patients with moderate and severe insomnia. Insomnia or moderate to severe insomnia has been

Table 1
Demographic and Clinical Characteristics and Insomnia Status

Characteristic	Insomnia Severity Index (N = 575)				
	No Insomnia (n = 198)	Mild Insomnia (n = 120)	Moderate Insomnia (n = 173)	Severe Insomnia (n = 84)	*P* Value
Age, y	72.9 ± 7.8	72.1 ± 7.2	74.2 ± 8.0	72.8 ± 7.8	.151
Gender, female,* %	60.6	78.3	80.9	79.8	**<.001**
Education, y*	4.5 ± 3.9	3.3 ± 2.9	2.5 ± 3.4	2.6 ± 3.2	**<.001**
CCI*	0.8 ± 1.1	0.8 ± 0.7	2.2 ± 9.3	1.1 ± 1.6	**<.05**
Number of drugs*	3.7 ± 2.6	4.4 ± 2.6	4.3 ± 2.6	5.1 ± 3.3	**.005**
Obesity, %	59.1	65.0	57.8	57.1	.338
Comorbidities, %					
Cerebrovascular events	6.1	1.7	6,9	7.1	.170
Diabetes mellitus	31.8	39.2	37.0	32.1	.493
Ischemic heart disease	12.2	15.8	15.0	16.7	.709
Congestive heart failure	4.5	4.2	7.0	9.5	.304
Hypertension	67.2	69.2	69.4	64.3	.848
COPD	9.6	10.0	12.7	19.0	.134
Osteoarthritis	22.2	26.7	30.6	25.0	.326
Parkinson's disease	3.5	5.0	6.4	7.14	.078
Dementia	5.1	3.3	5.2	7.1	.903
Depression*	38.6	35.6	59.2	62.3	**<.001**
MMSE*	25.6 ± 3.2	24.6 ± 4.4	22.9 ± 5.4	23.8 ± 3.8	**<.001**
Nutritional determinants					
Nutritional status*					
Malnutrition	1.5	5.8	10.4	7.1	**<.001**†
Risk of malnutrition	22.7	30.0	43.4	52.3	
Well-nourished	78.8	64.2	46.2	40.6	
MNA scores	25.4 ± 3.0	24.4 ± 3.4	22.7 ± 4.0	22.6 ± 3.3	**<.001**†
Classification of vitamin D, %					
≤10 ng/mL	34.3	49.2	42.8	38.1	.266
10-20 ng/mL	24.2	18.3	22.0	32.1	
>20 ng/mL	41.5	32.5	35.2	29.8	
Serum vitamin D levels	20.7 ± 16.7	18.0 ± 11.7	17.0 ± 11.7	18.1 ± 12.9	.709
Classification of vitamin B_{12}, %					
<200 pg/mL	14.1	13.3	15.0	12.2	.934
200-400 pg/mL	48.0	42.5	46.8	50.0	
>400 pg/mL	37.9	44.2	38.2	37.8	
<150 pg/mL	21.2	18.3	17.3	16.7	.793
≥150 pg/mL	78.8	81.7	82.7	83.3	
Serum vitamin B_{12} levels	267.3 ± 157.2	229.4 ± 119.3	277.1 ± 158.0	267.4 ± 166.5	.098
Serum folate levels	8.7 ± 3.6	9.0 ± 3.2	8.9 ± 3.2	9.6 ± 4.1	.518
Classification of folate, %					
<3 ng/mL	3.2	1.7	1.9	2.5	NA‡

Note. Bold values are statistically significant ($P < .05$).
CCI, Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease; MMSE, Mini-Mental State Examination; NA, not applicable.
*The parameters were significantly different between patients with insomnia (ISI score ≥8) and control group (ISI score <8).
†After adjustment for gender, education, number of drugs, CCI, presence of depression, and MMSE scores, *P* value was still found to be significant ($P < .05$).
‡The number of patients with folate deficiency was so low that it was not able to be analyzed.

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Table 2
Associations Between Nutritional Status and Insomnia Severity Status

Logistic Regression	Insomnia		Mild Insomnia		Moderate Insomnia		Severe Insomnia	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Malnutrition and risk of malnutrition	1.6 (0.9-2.7)	.070	1.8 (0.8-4.1)	.124	1.6 (1.0-2.5)	.046	1.6 (1.0-2.7)	.042
MNA scores	0.84 (0.7-0.9)	<.001	0.9 (0.8-1.0)	.051	0.83 (0.7-0.9)	<.001	0.82 (0.7-0.9)	<.001
Linear Regression	**Beta**	***P***	**Beta**	***P***	**Beta**	***P***	**Beta**	***P***
Malnutrition	0.348	<.001	0.135	.39	0.508	<.001	0.440	.02
Risk of malnutrition	0.213	<.001	0.097	.12	0.261	<.001	0.304	.04
MNA scores	−0.285	<.001	−0.022	.09	−0.358	<.001	−0.383	<.001

CI, confidence interval; OR, odds ratio.

shown to be significantly correlated with nutritional status and associated with low MNA scores. However, for mild insomnia, this relationship was not detected.

Insomnia is common in older adults, but the prevalence of both insomnia and moderate and severe insomnia in our study was more frequent than previous studies.[25] In a meta-analysis, the prevalence of sleep problems was found to be high in low- and middle-income countries and was associated with depression, low education, and low socioeconomic status, which may explain the high insomnia prevalence in our study.[26] In addition to this high incidence of insomnia, it may be associated with difficulty in maintaining daily activities, falling, fractures, stroke, physical disability, dementia, respiratory symptoms, and cardiac diseases.[3] Moreover, considering that the drugs used for the treatment of insomnia in older adults have numerous side effects, the importance of revealing the causes of reversible insomnia, which may lead to insomnia, will be better understood.[6]

Malnutrition or the risk of malnutrition, such as insomnia, is 1 of the most important geriatric syndromes that may cause complications similar to that of insomnia with increasing age; however, there is no study investigating how insomnia is affected by the nutritional status of patients. In our study, it was found that MNA scores and normal nutritional status were lower in patients with insomnia, particularly in patients with moderate and severe insomnia. Possible mechanisms that explain this may include the following: first, malnutrition may cause neurodegeneration and white matter damage, which may impair the regulation of brain functions.[27–29] For example, in previous studies, dialysis patients with anorexia nervosa and severe weight loss had a higher risk of the brain atrophy and low fat mass was associated with more white matter hyperintensities (WMHs).[28] In a study by Marian et al, it was claimed that in older adults malnutrition may cause WMHs rather than brain atrophy, which may be explained by the fact that malnutrition alone impairs cardiovascular homeostasis independently of other cardiovascular risk factors, as in our study.[29,30] Additionally, malnutrition-related inflammation is another cause of WMHs.[31] In recent years, these WMHs have been found to cause insomnia by disrupting the integrity between the left thalamus and pars triangularis tracts.[32] In another study, the dysfunctions of white matter structural network connectivity in healthy adults were found to be associated with insomnia symptoms.[33] On the other hand, experimental studies have shown that in rats with malnutrition, the size of the suprachiasmatic nucleus, which is the most powerful pacemaker for circadian rhythm, has a key role in sleep physiology, and that sleep deprivation is decreased by energy and nutritional supplementation.[34,35] Second, dietary factors can affect melatonin release.[36] Melatonin is a circulating neurohormone that is mainly secreted at night and is produced from tryptophan, an essential amino acid.[35] It is important to detect the daily light and dark cycle, so that the circadian rhythm can be regulated and help us fall asleep and stay asleep.[36] There are many studies showing the effect of diet on the synthesis or concentration of melatonin. For example, it has been shown in human studies that energy restriction decreases the release of melatonin at night.[36–39] In short-term (2 days) fasting healthy men, melatonin secretion was decreased compared to the control group,

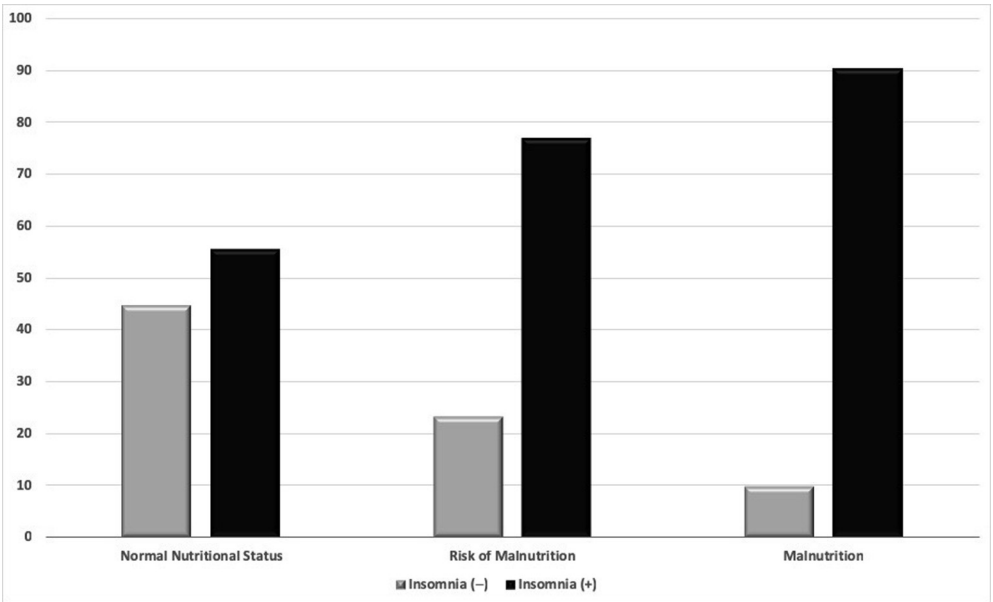

Figure 1. The relationship between Nutritional Status and Insomnia.

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and normalization of melatonin levels were found after glucose supplementation.[39] Similar studies have been made in obese individuals, and the same results have been obtained.[38] Third, in patients with malnutrition, orexin, a neuropeptide released from the hypothalamus to increase nutrition, also increases alertness.[40,41] Accordingly, a large number of studies have shown that sleep is adversely affected in patients with anorexia and bulimia nervosa compared to those without; therefore, sleep is thought to be a clinical marker for eating disorders.[42] Orexin neurons "fire" with circadian rhythm; thus, serum orexin levels increase during periods of wakefulness but decrease during sleep. A recent study demonstrated that plasma orexin levels were higher in patients with insomnia than those without insomnia.[43] Orexin receptor antagonists also were shown to improve sleep and might be potential pharmacologic agents for treatment of disordered eating in humans.[44,45] However, further research is necessary to address this issue. Lastly, insomnia itself may also affect dietary behaviors and intake.[46] For example, decreased appetite for heart failure patients was associated with insomnia.[47] On the other hand, decreased sleep time may also help to explain the cause of worsening nutrient status by increasing insomnia severity.[48] However, future studies utilizing a longitudinal or experimental design are needed to establish the accuracy of all these hypotheses.

Our study is the first to investigate insomnia severity and nutritional status in older adults. So far, the correlation between malnutrition and insomnia in older adults was vaguely mentioned in studies investigating geriatric syndromes associated with malnutrition, but this correlation could not elaborately be evaluated because they were not aimed for this purpose.[49,50] Although some studies have shown that vitamin B_{12}, folate, and especially vitamin D may cause insomnia,[10,11] it is unclear whether this relationship is due to malnutrition or indeed nutrient deficiency, because none of these studies concurrently have nutritional status assessed.

The strengths of our study are as follows: the number of adequate samples; grading not only the presence of insomnia but also the severity of insomnia; MNA—long form applied to all patients; and simultaneous evaluation of both nutritional and vitamin B_{12}, folate, and vitamin D. However, our study is not without limitation. First, the present study was cross-sectional in design, and the direction of the association is not known. That is, it is not known whether insomnia leads to poor nutritional parameters or whether poor nutritional parameters lead to insomnia. It is possible that the relationship is bidirectional. Future research of an experimental prospective design is now needed. Second, only the insomnia severity index scale was used for insomnia; hence, future studies should consider using objective measures of sleep to diagnose insomnia, such as actigraphy. Third, the correlations between MNA items associated with food intake or weight/weight loss variables and insomnia were not evaluated. Last, the number of patients with folate deficiency was so low that it was not able to be analyzed.

Conclusions and Implications

In conclusion, there is a close relationship between insomnia or insomnia severity and nutritional status in older adults. Especially in patients with moderate and severe insomnia, the MNA scores are lower. Therefore, when evaluating an older patient with insomnia in geriatric practice, malnutrition should be evaluated or insomnia should be investigated in an older patient with malnutrition. Thus, more effective management of the 2 will be possible.

References

1. Yaremchuk K. Sleep disorders in the elderly. Clin Geriatr Med 2018;34:205–216.
2. Patel D, Steinberg J, Patel P. Insomnia in the elderly: A review. J Clin Sleep Med 2018;15:1017–1024.
3. Foley DJ, Monjan A, Simonsick EM, et al. Incidence and remission of insomnia among elderly adults: An epidemiologic study of 6,800 persons over three years. Sleep 1999;22:S366–S372.
4. Gulia KK, Kumar VM. Sleep disorders in the elderly: A growing challenge. Psychogeriatrics 2018;18:155–165.
5. Kamel NS, Gammack JK. Insomnia in the elderly: Cause, approach, and treatment. Am J Med 2006;119:463–469.
6. Kalan U, Soysal P, Isik AT. Delirium associated with only one dose of zopiclone in an older adult. Psychogeriatrics 2018;18:321–323.
7. Soysal P, Smith L, Capar E, et al. Vitamin B_{12} and folate deficiencies are not associated with nutritional or weight status in older adults. Exp Gerontol 2018;116:1–6.
8. Soysal P, Turan Isik A. Vitamin B_{12} deficiency can be a cause of acute reversible parkinsonism and cognitive impairment in older adults. Geriatr Gerontol Int 2018;18.
9. Ates Bulut E, Soysal P, Aydin AE, et al. Vitamin B_{12} deficiency might be related to sarcopenia in older adults. Exp Gerontol 2017;95:136–140.
10. Beydoun MA, Gamaldo AA, Canas JA, et al. Serum nutritional biomarkers and their associations with sleep among US adults in recent national surveys. PLoS One 2014;9:e103490.
11. Massa J, Stone KL, Wei EK, et al. Vitamin D and actigraphic sleep outcomes in older community-dwelling men: The MrOS Sleep Study. Sleep 2015;38:251–257.
12. Grandner MA, Jackson N, Gerstner JR, Knutson KL. Sleep symptoms associated with intake of specific dietary nutrients. J Sleep Res 2014;23:22–34.
13. Unutmaz GD, Soysal P, Tuven B, Isik AT. Costs of medication in older patients: Before and after comprehensive geriatric assessment. Clin Interv Aging 2018;13:607–613.
14. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. J Chronic Dis 1987;40:373–383.
15. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Washington, DC: American Psychiatric Association; 2013.
16. Dokuzlar O, Soysal P, Usarel C, Isik AT. The evaluation and design of a short depression screening tool in Turkish older adults. Int Psychogeriatr 2018;30:1541–1548.
17. Güngen C, Ertan T, Eker E, et al. Reliability and validity of the standardized Mini Mental State Examination in the diagnosis of mild dementia in Turkish population. Türk Psikiyatr Derg 2002;13:273–281.
18. Vellas B, Guigoz Y, Garry PJ, et al. The Mini Nutritional Assessment (MNA) and its use in grading the nutritional state of elderly patients. Nutrition 1999;15:116–122.
19. Cereda E. Mini nutritional assessment. Curr Opin Clin Nutr Metab Care 2012;15:29–41.
20. Bastien CH, Vallières A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. Sleep Med 2001;2:297–307.
21. Morin CM, Belleville G, Bélanger L, Ivers H. The Insomnia Severity Index: Psychometric indicators to detect insomnia cases and evaluate treatment response. Sleep 2011;34:601–608.
22. Bozoglu E, Isik AT, Doruk H, Kilic S. The effects of early vitamin B_{12} replacement therapy on the cognitive and functional status of elderly subjects. Klin Psikofarmakol Bul 2010;20:120–124.
23. Abeywickrama HM, Koyama Y, Uchiyama M, et al. Micronutrient status in Sri Lanka: A review. Nutrients 2018;10:1583.
24. Thacher TD, Clarke BL. Vitamin D insufficiency. Mayo Clin Proc 2011;86:50–60.
25. Dragioti E, Bernfort L, Larsson B, et al. Association of insomnia severity with well-being, quality of life and health care costs: A cross-sectional study in older adults with chronic pain (PainS65+). Eur J Pain 2018;22:414–425.
26. Mazzotti DR, Guindalini C, Sosa AL, et al. Prevalence and correlates for sleep complaints in older adults in low and middle income countries: A 10/66 Dementia Research Group study. Sleep Med 2012;13:697–702.
27. Mukai M, Mukai K, Ichikawa H, et al. Malnutrition and cerebral white matter lesions in dialysis patients. Nippon Toseki Igakkai Zasshi 2008;41:421–428.
28. Fleta Zaragozano J, Jiménez Vidal A, Velilla Picazo M, et al. Anorexia nervosa and cerebral atrophy in adolescents [in Spanish]. Med Clin (Barc) 2005;124:571–572.
29. de van der Schueren MAE, Lonterman-Monasch S, van der Flier WM, et al. Malnutrition and risk of structural brain changes seen on magnetic resonance imaging in older adults. J Am Geriatr Soc 2016;64:2457–2463.
30. Handler PBF. Influence of dietary factors on hypertension induced by choline deficiency. Am J Physiol 1950;162:189.
31. Zheng K, Wang H, Hou B, et al. Malnutrition-inflammation is a risk factor for cerebral small vessel diseases and cognitive decline in peritoneal dialysis patients: A cross-sectional observational study. BMC Nephrol 2017;18:366.
32. Kang JM, Joo SW, Son Y-D, et al. Low white-matter integrity between the left thalamus and inferior frontal gyrus in patients with insomnia disorder. J Psychiatry Neurosci 2018;43:366–374.
33. Lu F-M, Dai J, Couto TA, et al. Diffusion tensor imaging tractography reveals disrupted white matter structural connectivity network in healthy adults with insomnia symptoms. Front Hum Neurosci 2017;11:583.
34. Cintra L, Galvan A, Diaz-Cintra S, Escobar C. Protein malnutrition on suprachiasmatic nucleus cells in rats of three ages. Bol Estud Med Biol 1994;42:11–19.
35. Everson CA. Functional consequences of sustained sleep deprivation in the rat. Behav Brain Res 1995;69:43–54.

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36. Peuhkuri K, Sihvola N, Korpela R. Dietary factors and fluctuating levels of melatonin. Food Nutr Res 2012;56:17252.
37. Michalsen A, Schlegel F, Rodenbeck A, et al. Effects of short-term modified fasting on sleep patterns and daytime vigilance in non-obese subjects: Results of a pilot study. Ann Nutr Metab 2003;47:194–200.
38. Röjdmark S, Rössner S, Wetterberg L. Effect of short-term fasting on nocturnal melatonin secretion in obesity. Metabolism 1992;41:1106–1109.
39. Rojdmark S, Wetterberg L. Short-term fasting inhibits the nocturnal melatonin secretion in healthy man. Clin Endocrinol (Oxf) 1989;30:451–457.
40. Mossavar-Rahmani Y, Jung M, Patel SR, et al. Eating behavior by sleep duration in the Hispanic Community Health Study/Study of Latinos. Appetite 2015;95:275–284.
41. Allison KC, Spaeth A, Hopkins CM. Sleep and eating disorders. Curr Psychiatry Rep 2016;18:92.
42. Asaad Abdou T, Esawy HI, Abdel Razek Mohamed G, et al. Sleep profile in anorexia and bulimia nervosa female patients. Sleep Med 2018;48:113–116.
43. Tang S, Huang W, Lu S, et al. Increased plasma orexin-A levels in patients with insomnia disorder are not associated with prepro-orexin or orexin receptor gene polymorphisms. Peptides 2017;88:55–61.
44. Sun H, Kennedy WP, Wilbraham D, et al. Effects of suvorexant, an orexin receptor antagonist, on sleep parameters as measured by polysomnography in healthy men. Sleep 2013;36:259–267.
45. Cole S, Mayer HS, Petrovich GD. Orexin/hypocretin-1 receptor antagonism selectively reduces cue-induced feeding in sated rats and recruits medial prefrontal cortex and thalamus. Sci Rep 2015;5:16143.
46. Kim S, Deroo LA, Sandler DP. Eating patterns and nutritional characteristics associated with sleep duration. Public Health Nutr 2011;14:889–895.
47. Andreae C, Strömberg A, Årestedt K. Prevalence and associated factors for decreased appetite among patients with stable heart failure. J Clin Nurs 2016;25:1703–1712.
48. Jung CM, Melanson EL, Frydendall EJ, et al. Energy expenditure during sleep, sleep deprivation and sleep following sleep deprivation in adult humans. J Physiol 2011;589:235–244.
49. El-Desouky R, Abed H. Screening of malnutrition and its correlates among a sample of rural elderly in Qalyobeya Governorate, Egypt. J Egypt Public Health Assoc 2017;92:156–166.
50. Saka B, Kaya O, Ozturk GB, et al. Malnutrition in the elderly and its relationship with other geriatric syndromes. Clin Nutr 2010;29:745–748.

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