Impact of Poor Sleep on Physical and Mental Health in Older Women

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KEYWORDS

• Sleep deficiency • Circadian rhythms • Cardiometabolic disorders • Older women • Metabolic syndrome • Physical health • Mental health • Falls

KEY POINTS

- The prevalence of sleep disorders and disturbances increases with age and older women may be more sensitive to the impact of aging on sleep.
- Short sleep duration, poor sleep quality, insomnia, sleep-disordered breathing, and weakened rest–activity rhythms are associated with adverse cardiometabolic outcomes, including obesity, metabolic disorders, and cardiovascular disease.
- Sleep disorders and disturbances, and weakened rest–activity rhythms, are associated with adverse mental health outcomes, including increased risk of depressive symptoms, dementia, and cognitive decline.
- Disturbances in sleep and treatments for sleep contribute to other outcomes, such as falls, disability, and chronic pain.
- Clinicians should consider special needs of older women in the diagnosis and treatment of sleep problems.

INTRODUCTION

Sleep is an important determinant of human health, and healthy sleep is crucial for healthy aging. In a recent joint consensus statement of the American Academy of Sleep Medicine and Sleep Research Society, healthy sleep was defined as "adequate duration, good quality, appropriate timing and regularity, and the absence of sleep disturbances or disorders."[1] The prevalence of sleep disorders and disturbances increases dramatically with advancing age.[2] There is growing evidence that sleep disturbances may accelerate the aging process and contribute to a wide range of chronic diseases. Despite these health consequences, sleep problems frequently are undiagnosed and untreated, particularly in the elderly.[3]

Previous studies have suggested that, compared with men, women may be more sensitive to the impact of aging on sleep and older women are more likely to report sleep problems.[4,5] As the older population continues to grow in many parts of the world, it is important to understand the health effects of sleep disruption in the context of aging. This review synthesizes and presents epidemiologic and clinical evidence on the relationships between sleep deficiency and various health conditions that are highly prevalent in older

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women, explores potential mechanisms underlying such relationships, points out gaps in the literature that warrant future investigations, and considers implications for the clinical and public health settings.

SLEEP IN OLDER ADULTS

Many aspects of sleep change as people age. A 2004 meta-analysis by Ohayon and colleagues[6] synthesized findings from 65 studies with objective measurement of sleep using polysomnography (PSG) or actigraphy. They found that older age was associated with decreases in total sleep time, sleep efficiency and percentage of slow-wave sleep and rapid eye movement sleep; whereas sleep latency, percentage of light sleep, and minutes of wake after sleep onset significantly increased with age. Such changes in sleep architecture are consistent with an increase in sleep complaints in the older population. In more than 9000 people aged 65 years or older, Foley and colleagues[7] assessed the frequencies of reporting common sleep disturbances, including trouble falling asleep, waking up, waking too early, and nonrestorative sleep. In this study, half of the participants reported at least 1 complaint as frequently occurring, and up to a third of the population showed symptoms of insomnia.[7] Similarly high prevalence (15%–25%) of insomnia symptoms has also been reported in the Sleep Heart Health Study (SHHS).[8] Sleep-disordered breathing (SDB), another common sleep disorder, is estimated to affect from 30% to 60% of older adults, depending on the definition used and specific population.[9–13] Moreover, aging coincides with altered circadian activity rhythms, including decreased amplitude (height of rhythm),[14] fragmentation or loss of rhythms (weakening of rhythmic pattern),[15,16] and altered timing of peak rhythm activity. Timing changes in older adults frequently result in earlier onset of sleepiness in the evening and an earlier morning waking time.[16]

Interestingly, a growing body of evidence suggests that there are sex differences both in sleep and age-related changes in sleep.[4] In general, although women tend to have better objectively measured sleep quality, paradoxically, they are more likely than men to report subjective sleep problems, including shorter sleep and poorer sleep quality.[17] A meta-analysis of sex differences in insomnia showed that not only is the risk of insomnia higher in women than in men across all age groups, the difference in insomnia risk between women and men widens with age.[18]

SLEEP AND CARDIOMETABOLIC HEALTH

Sleep plays a vital role in numerous physiologic processes, including the regulation of metabolic, hormonal, and immune function, all of which are essential for cardiometabolic health. Numerous studies have linked disorders and disturbances of sleep to cardiometabolic outcomes, including obesity, hypertension, dyslipidemia, diabetes, and cardiovascular disease (CVD).

Sleep Duration

Short sleep duration is associated with obesity in children and younger adults; however, such a relationship in older adults remains less clear.[19–21] The mixed findings in the elderly may be partially due to the high prevalence of chronic conditions in this population, which may both confound and modify the effect of sleep on weight. In a study of more than 80,000 healthy men and women aged 51 to 72 years, those with self-reported short sleep (<7 hours) at baseline were more likely to experience substantial weight gain (≥5 kg) and risk of developing obesity over 10 years of follow-up.[22] Interestingly, this association may be stronger in older women than in men. Two studies of middle-to-old-aged subjects in Finland and Spain reported an association between short sleep and higher weight gain in women but not in men.[23,24]

Short sleep duration has also been associated with other cardiometabolic consequences. Two meta-analyses showed that short sleep duration was associated with a 23% increase in hypertension risk,[25] a 48% increase in coronary heart disease, and a 15% increase in stroke,[26] and these associations were stronger in women. Another meta-analysis demonstrated that each 1-hour decrease in sleep duration was associated with a significant 9% increase in the risk of type 2 diabetes.[27]

Several studies have also reported an association between long sleep duration and obesity, diabetes, and CVD risk and mortality.[26,28] In a large observational study of older women, Stone and colleagues[29] found that those who reported 10 or more hours of sleep per 24 hours had a 77% increase in risk of cardiovascular-related mortality compared with older women who reported 8 to 9 hours of sleep. Several lines of evidence suggest that these associations with adverse health outcomes related to long sleep duration may be partially explained by comorbidities.[30–32]

Studies using objectively measured sleep duration in the older population are still limited and their findings are mixed. For example, a cross-sectional relationship between objectively measured short

sleep and higher adiposity was observed in both the Multi-Ethnic Study of Atherosclerosis and the Study of Osteoporotic Fractures (SOF).[33,34] However, thus far, prospective analyses in younger adults have found no relationship between actigraphy-measured short sleep duration and weight gain.[35,36]

Insomnia and Poor Sleep Quality

Several studies reported greater adiposity associated with various measures of sleep quality, such as wakefulness, sleep fragmentation, daytime sleepiness, and overall poor sleep quality.[37–40] van den Berg and colleagues[39] found that greater objectively measured sleep fragmentation was associated with higher body mass index and greater risk of obesity in older adults. In addition, the association between short sleep duration and obesity was no longer significant after adjustment for sleep fragmentation. This suggests that, in older adults, the quality of sleep may be more important than the quantity in relation to cardiometabolic outcomes. Poor sleep quality, measured both subjectively and objectively, has also been linked to several markers of subclinical CVD,[41] as well as poorer glycemic control measured by increased hemoglobin A_{1c} in patients with type 2 diabetes.[42] However, Phillips and colleagues[43] found no association of insomnia symptoms with incident hypertension in older women.

Finally, some studies have suggested that objectively measured short sleep duration and insomnia symptoms together increase risk of CVD more strongly than either condition alone. For example, Bertisch and colleagues[44] examined short sleep (objectively measured based on PSG), insomnia, or poor sleep quality, and the interaction of these sleep problems for prediction of incident CVD in middle-aged to older adults. Although neither condition alone was significantly associated with incident CVD, those with both short sleep and insomnia or poor sleep quality had a significant 30% increase in risk of incident CVD over 11 years of follow-up. These results were similar in both women and men. This finding highlights the importance of considering sleep health as a multidimensional exposure in terms of the affect on health in aging.

Snoring and Sleep-Disordered Breathing

There is a well-established association between SDB and obesity, as well as obesity-related health outcomes.[45] In addition, several studies also showed that even occasional snoring may be a risk factor for obesity, metabolic syndrome, and diabetes in middle-to-old aged women.[46,47] Among middle-aged women in the Nurses' Health Study, those who reported occasional snoring were 40% more likely to develop diabetes during 10 years of follow-up than those who reported never snoring.[46]

Epidemiologic studies have also established that SDB increases the risk for incident hypertension, heart failure, coronary heart disease, and stroke in men and younger adults.[48–50] However, effects of SDB on cardiovascular outcomes in older women are uncertain. Early findings from the SHHS showed associations with CVD only in men, whereas more recent data from the SHHS and Atherosclerotic Risk in Communities cohorts showed that SDB severity predicted higher troponin levels and increased risk for left ventricular hypertrophy, heart failure, and CVD-related mortality among elderly women compared with men.[51] These data, which focused on an older sample for a longer period of time than earlier analyses, underscore the importance of examining this risk in older women.

Weakened Rest–Activity Rhythms

Circadian rhythms are intrinsic physiologic cycles of approximately 24 hours that are critically involved in control of sleep–wake cycles and numerous physiologic processes. Circadian and sleep–wake rhythm abnormalities have been observed among those with a wide variety of medical conditions. However, it is not clear whether sleep–wake rhythms directly influence morbidity and mortality in aging, or are biomarkers of advanced physiologic age. Indeed, van Hilten and colleagues[52] studied the relationship of age with nocturnal behavior in 100 healthy older adults and found that, in the absence of illness, age itself has only marginal effects on sleep and wake.

Using actigraphy, a previous study of older women in the SOF found that lower amplitude, extreme timing (early or late) of peak activity, and weaker strength in the overall rhythmicity predicted higher cardiovascular mortality.[53] Similarly, a more fragmented and less stable rhythm of rest and activity was associated with total mortality in the Rotterdam Study, although the study did not specifically examine cardiovascular deaths.[54]

SLEEP AND DEPRESSION

Although the prevalence of major depression in older adults is relatively low at 1% to 2%, an increasing number of older adults experience clinically significant depressive symptoms[55] that are linked to greater risk of functional impairment, disability, and illness.[56] Furthermore, late-life depression disproportionately affects older

women. Some evidence suggests that this is because older women tend to experience more persistent depressive symptoms over time and have longer survival compared with men.[55,57]

Sleep Duration

Cross-sectional studies have reported greater prevalence of depressive symptoms in older adults with both short and long sleep duration.[30,57,58] Although a protective role for sleep deprivation or short sleep in risk of depression has been reported in younger adults, these findings have not been confirmed in older adults.[59,60] Using data from the Nurses' Health Study, Patel and colleagues[30] found that depressive symptoms were strongly correlated with self-reported long sleep duration. Another study reported that an association between self-reported long sleep duration and depressive symptoms was significant in older men but not older women.[57]

Fewer studies have examined the association of sleep duration and the risk of developing depressive symptoms over time. A few longitudinal studies using both objective and subjective assessment of sleep in older adults have reported no significant association of sleep duration (either short or long) and risk of incident depressive symptoms.[61,62] However, Fernandez-Mendoza and colleagues[61] studied a cohort of adults (mean age 52 years) and found that those with insomnia and objectively measured short sleep duration had the highest risk of developing depressive symptoms over 7.5 years of follow-up. This finding further underscores the importance of considering sleep health more comprehensively rather than focusing on a single domain.

Insomnia and Poor Sleep Quality

Insomnia is common in older adults with depression but recent evidence suggests that this is a bidirectional association and that insomnia and poor sleep quality may also lead to incident depressive symptoms over time. For example, Maglione and colleagues[62] studied 952 women aged 70 years and older with minimal depressive symptoms at baseline. Sleep was assessed objectively using actigraphy and subjectively using the Pittsburgh Sleep Quality Index (PSQI). Higher PSQI scores (indicating more sleep disturbance) were associated with greater risk of developing depressive symptoms, with stronger associations for the sleep quality (OR 1.41, CI 1.13–1.77) and sleep latency (OR 1.21, CI 1.03–1.41) subscales. Objectively, prolonged minutes of wake after sleep onset emerged as a risk factor for incident depressive symptoms, whereas sleep duration was not a significant predictor. These findings suggest that sleep quality, rather than the absolute quantity of sleep, may be more important for mental health in older women.

The effects of poor sleep on risk of depressive symptoms may not be limited to a single domain of sleep (eg, sleep duration). Furihata and colleagues[63] tested the association of an index of sleep health in relation to risk of incident depressive symptoms in older women. The 0 to 5 index was created by summing across 5 dimensions classified as poor, based on self-reported sleep, including satisfaction with sleep duration, daytime sleepiness, midsleep time, sleep onset latency, and sleep duration. Results showed a strong gradient of increasing risk of developing incident depressive symptoms with increasing number of poor sleep dimensions. Despite these intriguing findings, the body of evidence linking sleep to depression has tended to focus on 1 dimension at a time.

Weakened Rest–Activity Rhythms

Although aging promotes disruption in circadian rhythms, the relationship between depression and circadian rhythm disruption in older adults remains largely unexplored. Maglione and colleagues[64] examined the relationship between depressive symptoms and circadian activity rhythms in older adults among 3020 women (mean age 84 years). Greater levels of depressive symptoms were associated with greater desynchronization of circadian activity rhythms, as well as later average time becoming active in the morning; however, there was no association with acrophase. Further evidence of an association between circadian activity rhythms and risk of depression was reported in a longitudinal analysis by Smagula and colleagues.[65] Among 2124 older men with minimal depressive symptoms at baseline, those in the lowest quartile of rhythm robustness were 2.5 times more likely to develop clinically significant depressive symptoms during a 5-year follow-up (odds ratio [OR] 2.58, 95% CI 1.11–5.59). Rhythm timing and amplitude did not significantly predict development of depression. These associations have not been examined in older women.

SLEEP, COGNITIVE DECLINE, AND RISK OF DEMENTIA

Sleep disturbance is common in older adults with dementia, and evidence suggests that disturbed sleep may contribute to development of cognitive problems and risk of dementia.[66] Although the

mechanisms are not completely understood, experimental studies suggest that even a single night of sleep deprivation leads to accumulation of beta-amyloid in the human brain.[67] Beta-amyloid is a metabolic waste product that may form plaques over time, contributing to Alzheimer disease. Sleep may, therefore, play a critical role in the prevention of cognitive decline and risk for Alzheimer disease. Evidence also suggests that SDB may pose a risk for development of cognitive problems in older women.

Sleep Duration and Poor Sleep Quality

Overall, there is little prospective evidence of an association between sleep duration and cognitive decline or risk of incident dementia. Chen and colleagues[68] studied 7444 community-dwelling older women to test whether self-reported sleep duration predicted incident mild cognitive impairment (MCI) or dementia during follow-up. They found a V-shaped association between sleep duration and risk of MCI or dementia, with both short ($\leq$6 hours per night) and long ($\geq$8 hours per night) sleepers showing 35% to 36% increase in risk.[68] However, other studies of both older men and women with actigraphy measures of sleep demonstrated no association of sleep duration and risk of cognitive decline.[69,70] In contrast, these studies showed that objective measures of sleep fragmentation (eg, sleep efficiency) consistently predicted both cross-sectional cognitive function, as well as prospective decline in cognition. Further studies are needed to better define the characteristics of healthy sleep that may prevent cognitive decline in older women, and to determine if treatment of sleep problems may slow the decline in cognition and development of dementia.

Snoring and Sleep-Disordered Breathing

SDB results in nocturnal hypoxemia and more fragmented sleep, both of which may have effects on cognitive function. Yaffe and colleagues[71] studied the association of SDB and nocturnal hypoxemia (assessed using overnight in-home PSG) with subsequent 5-year risk of developing MCI and dementia among 298 older women (mean age 82.3 years). In this study, older women with SDB (apnea-hypopnea index $\geq$15) had nearly a 2-fold increase in the risk of developing MCI or over 5 years of follow-up, whereas nocturnal hypoxemia was associated with a 1.71-fold increase in risk of developing MCI or dementia.[71] In another study, Chang and colleagues[72] used data from a large health insurance database in Taiwan to compare 5-year risk of dementia among adults aged 40 year and older with and without sleep apnea diagnosis at baseline. Among the 1414 subjects studied, presence of sleep apnea was associated with a significant 1.7-fold increase in risk of developing dementia. In this same study, sleep apnea diagnosis was associated with a 3.2-fold increase in risk of incident dementia in women aged 70 years and older.[72]

There is insufficient evidence for an association between snoring and risk of cognitive decline or onset of dementia.

Weakened Rest–Activity Rhythms

Tranah and colleagues[73] examined whether circadian activity rhythms (based on actigraphy) were associated with incident MCI and dementia over 5 years in 1282 older women. An approximately 50% adjusted higher odds of developing dementia or MCI versus those without any dementia or MCI was observed for those in the lowest quartile of amplitude and rhythm robustness when compared with those in the highest quartile. Timing of activity rhythms also predicted incident MCI or dementia. In particular, older women with delayed acrophase (>1.5 standard deviations of the population mean) had a significant increase in odds of developing dementia or MCI (OR 1.83, 95% CI, 1.29–2.61) when compared with the mean peak range (mean $\pm$ 1.5 standard deviations).

SLEEP AND OTHER AGE-RELATED OUTCOMES AND CONDITIONS

Disturbed sleep in older women, and hypnotics used to treat sleep problems, are independently associated with risk of incident falls.[74–76] Falls are common in older adults, and frequently lead to injury and increased disability[77] and mortality.[78] Further evidence suggests that poor sleep may contribute to decline in physical functioning among older women, independent of falls.[79] Sleep disturbance is also common in older women with chronic pain, and more recent evidence suggests that this association is bidirectional and that sleep problems may increase the risk of developing chronic pain.[80] Treatment of insomnia symptoms using cognitive behavioral therapy in older adults with osteoarthritis showed that short-term (2 months) improvements in sleep predicted longer-term improvement in chronic pain outcomes over 9 to 18 months.

IMPLICATIONS FOR CLINICAL PRACTICE

Given the high prevalence of sleep problems in older women, and the debilitating impact on quality of life and physical and mental health, it is imperative for health care professionals to identify,

monitor, and treat sleep problems in this vulnerable population. Unfortunately, evidence suggests that, compared with other lifestyle behaviors, sleep problems have not been screened as frequently in family medicine clinics.[81] Special needs of older women should be considered in determining the best treatment options. In older women with sleep apnea, behavior modification, such as avoiding alcohol and certain medications, may be particularly important because these patients may be more sensitive to their effects on upper airway function during sleep.[82] Hypnotic medications are effective and commonly prescribed by physicians for treatment of insomnia but have been linked to adverse events in the elderly, including falls and fractures, adverse cognitive and psychomotor events, and daytime fatigue.[83] Therefore, the American Geriatric Society has recommended avoiding hypnotic prescriptions for insomnia in older adults.[84] Randomized controlled trails have shown that behavioral interventions, including cognitive behavioral therapy for insomnia, are effective in older adults[85] and should be considered as the first-line approach. Moreover, several studies also showed that exercise,[86,87] social activities,[88] and cognitive training[89] may also be beneficial for older adults with insomnia.

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