



Frailty and Insomnia in Older Adults

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Frailty is a geriatric syndrome with increased risk for poor health outcomes, including falls, cognitive impairment, hospitalization, and mortality. In previous studies, associations between frailty and sleep-related factors or sleep disorders have been investigated. We examined the relationship between frailty and insomnia, which are both common conditions in older adults. Hormonal changes with aging and/or lifestyle changes all affect sleep physiology, which are vulnerable to the risk of insomnia. As the severity of frailty decreases the quality of sleep, and the long/short sleep duration is related to the risk of frailty, it can be assumed that frailty and sleep are reciprocally related. The association between frailty and insomnia has been variously proven in epidemiological studies conducted around the world. A close evaluation of insomnia and frailty in older adults provides a basis for improving the health of people in the aged society. There are few related studies in Korea, and in the future, not only basic epidemiological studies but also studies explaining the psychoneuroendocrinological mechanism of the relationship between insomnia and frailty should be performed together.

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INTRODUCTION

Frailty is defined as a multidimensional geriatric syndrome that results from aging-associated functional and physiological decline [1]. Its phenotype includes unintentional weight loss, exhaustion, low physical activity, slowness, and weakness; it is associated with an increased risk of falls, hospitalization, morbidity, and mortality [2]. Sarcopenia is an elementary factor of frailty and is defined as a progressive reduction of mass and strength in the skeletal muscles [3].

Previous studies have revealed an independent association between frailty and sleep-disordered breathing [4,5]; the relationships between various frailty-related factors (e.g., sarcopenia) and sleep quality or duration have also been investigated [6-8]. In Korea, the prevalence of insomnia among community-dwelling older adults is approximately 20%–30% [9,10]; the prevalence of frailty among older adults is approximately 10%–20% less than that of insomnia [11,12]. Frailty and insomnia are both common conditions in older adults, so more research investigating them together is needed. However, few studies in Korea have examined the rela-

tionship between frailty and insomnia. As Soyeux [13] stated, the importance of research on aging and sleep in older adults is increasing. In this review, we focus on the relationship between frailty and insomnia, which is the most common sleep disorder in older adults.

CHANGES IN SLEEP PHYSIOLOGY WITH AGING

Although the total sleep duration in older adults is similar to or slightly decreased than that of younger adults, the duration of the deep-sleep stage is clearly reduced [14]. This phenomenon appears to be caused by changes in sleep parameters that accumulate in middle-aged adults [15]. Human circadian rhythms change as age increases, including a phase advance in the rhythm, reduced amplitude in the rhythm, and a decreased ability to adjust to phase shifting [15].

Fundamentally, the hormonal changes that occur with aging affect sleep. While several hormones are involved, including cortisol, prolactin, thyroid-stimulating hormone, and sex hormones

[16], the effects of growth hormone (GH) and melatonin are the most studied. GH secretion rapidly declines between young adulthood and middle age and then declines slowly between middle and old age; this is similar to the age-related decline in deep sleep. Meanwhile, nocturnal levels of melatonin in older adults are significantly lower than they are in younger adults [17]. This age-related decrease in melatonin secretion contributes to increased sleep disturbances in older adults.

In addition, age-related sleep changes such as sleep fragmentation or deep sleep reduction, lowered sleep efficiency, insomnia, sleep apnea, and circadian rhythm disruption are known to increase muscle catabolism and decrease muscle anabolism to increase the risk of sarcopenia, which is the main cause of the physical phenotype of frailty [18].

RELATIONSHIP BETWEEN FRAILITY AND SLEEP

Kaur et al. [19] reported that the degree of frailty is associated with cognitive decline, and sleep quality has a mediating effect on this relationship. In that study, more-severe frailty was significantly associated with poor sleep quality. When this was analyzed using a mediation model, processing speed was slower due to the effect of frailty on sleep quality; consequently, delayed-recall function was also worse. In a community cohort study of 2,505 men followed for 3.4 years, it was found that incident frailty was significantly associated with sleep quality, sleep latency, sleep efficiency, and sleep-disordered breathing [20]. In addition to sleep quality, there is also evidence that shorter or longer sleep periods are associated with physical, psychological, and socially frailty [21].

It can be assumed that frailty and sleep are reciprocally related. The link between sleep and frailty appears to be mediated by several factors, including decreased testosterone levels, chronic inflammation, imbalanced GH secretion, and the biochemical mechanisms associated with increased cortisol levels [18].

Frailty is associated with insulin resistance [22,23]; it is hypothesized that poor sleep quality affects the function of the central nervous system in frail older adults through exacerbation of insulin resistance. Sleep disturbances also have the potential to accelerate age-related changes in glucose tolerance [16]. In addition, sleep deprivation is associated with increased levels of oxidative stress markers in the liver. High levels of oxidative stress are associated with frailty [24].

On the other hand, low physical activity (a characteristic of frailty), excessive naps, and low exposure to sunlight may cause poor sleep hygiene, which may adversely affect nighttime sleep. There are many factors related to lifestyle or the environment that need to be considered when analyzing the relationship between frailty and insomnia.

A cross-sectional analysis of the cohort operated by the National Health and Aging Trends Study [25] revealed that pain, difficulty in initiating sleep, and depressive symptoms were independently associated with frailty in the older adults. According

to the study, the coexistence of two or more symptoms, such as depressive symptoms and pain, and depressive symptoms and insomnia, had a greater association with the development of pre-frailty and frailty than when only each single symptom was present [25]. The combined cross-sectional relationship with pain and depressive symptoms of frailty was 8.13 (odds ratio [OR]), which was larger than the sum of the each associations of pain (OR=1.41) and depressive symptom (OR=3.63). It can be assumed that each symptom causes a reciprocal action. Further studies will be needed on the specific mechanism of how these symptoms and frailty affect each other.

PREVIOUS EPIDEMIOLOGICAL STUDIES OF FRAILITY AND INSOMNIA

In this section, we review some recently published epidemiological studies on the relationship between frailty and insomnia.

A 2-year longitudinal study of 3,844 rural older adults in Japan found a bidirectional relationship between insomnia and frailty: insomnia predicted the onset and aggravation of frailty and, conversely, frailty predicted the severity of insomnia [26]. In men, the effect that frailty had on insomnia was greater than the effect that insomnia had on frailty. However, in women, the effect of insomnia on frailty was greater than the effect of frailty on insomnia. Sex-related differences in the association between frailty and insomnia have also been reported in studies conducted in other countries [27,28]. In a study by Moreno-Tamayo et al. [28], insomnia, poor sleep quality, and a sleep duration of less than 5 h were found to increase the risk of frailty in women; in men, multivariate logistic models found no significant association between insomnia and frailty. In previous studies, women showed higher levels than men did for inflammatory markers [29] and allostatic load [30], which are risk factors for frailty. Thus, at least in women, an insomnia-induced increase in inflammation may increase vulnerability to frailty.

In studies that examine insomnia in more detail, the evidence is slightly different even within the phenomena of insomnia. A study in Hong Kong found that frail older adults had a higher prevalence of sleep-onset insomnia compared to non-frail older adults; however, sleep-maintenance insomnia was not associated with frailty [31]. A study using data from the National Social Life, Health, and Aging Project found that the risk of frailty became greater as the sleep fragmentation index increased, as measured by three days of wrist actigraphy [32]. Vaz Fragoso et al. [33] found that daytime sleepiness was more strongly associated with frailty than the insomnia severity.

Together, this epidemiological evidence provides a basis for clinically evaluating insomnia and general sleep states more closely and for providing active intervention for both frail and non-frail older adults.

CONCLUSION

In this mini-review, we examined the relationship between frailty and insomnia in older adults. Frailty is related closely to not only the consequences of falls due to weakness of the musculoskeletal system, but also to the risk of dementia and mortality. In older adults (especially women), insomnia may induce or exacerbate frailty and, conversely, frailty may cause insomnia.

In addition to surveying the current epidemiological state of frailty and insomnia, it is recommended that research should be performed to elucidate the specific mechanisms that relate insomnia to frailty. In future studies, it will be necessary to examine the levels of cortisol, GH, melatonin, and inflammatory markers in regards to their psychoneuroendocrinological aspects. Furthermore, it seems necessary to study whether intervention for insomnia can prevent or slow the progression of frailty from a therapeutic perspective.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Availability of Data and Material

Data sharing not applicable to this article as no datasets were generated or analyzed during the study.

Author Contributions

Conceptualization: Woo Jung Kim, Eun Lee. Funding acquisition: Woo Jung Kim. Investigation: Woo Jung Kim, Kyung Mee Park. Supervision: Eun Lee. Writing—original draft: Woo Jung Kim. Writing—review & editing: Kyung Mee Park.

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