

Sleep disturbance in older ICU patients

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Abstract: Maintaining a stable and adequate sleeping pattern is associated with good health and disease prevention. As a restorative process, sleep is important for supporting immune function and aiding the body in healing and recovery. Aging is associated with characteristic changes to sleep quantity and quality, which make it more difficult to adjust sleep–wake rhythms to changing environmental conditions. Sleep disturbance and abnormal sleep–wake cycles are commonly reported in seriously ill older patients in the intensive care unit (ICU). A combination of intrinsic and extrinsic factors appears to contribute to these disruptions. Little is known regarding the effect that sleep disturbance has on health status in the oldest of old (80+), a group, who with diminishing physiological reserve and increasing prevalence of frailty, is at a greater risk of adverse health outcomes, such as cognitive decline and mortality. Here we review how sleep is altered in the ICU, with particular attention to older patients, especially those aged ≥ 80 years. Further work is required to understand what impact sleep disturbance has on frailty levels and poor outcomes in older critically ill patients.

Keywords: intensive care unit, sleep–wake rhythm, aging, frailty

Sleep and health

Adequate sleep and stable sleep–wake cycles are important to maintaining good lifelong physical and mental health. Chronically disrupting sleep and deviating the natural sleep–wake rhythm from the normal 24-hour environmental cycle can contribute to various long-term health consequences,¹ including obesity,² cardiovascular disease,³ and type 2 diabetes.⁴ In addition, disrupted sleep–wake rhythms (eg, chronic shift work) can strongly increase the risk for cancer.^{5,6} Sleep loss and disruption can also lead to weakened immune system function,^{7,8} diminished memory consolidation,⁹ disrupted neuroendocrine function, including changes in glucose metabolism,¹⁰⁻¹² and cognitive decline, including a diagnosis of Alzheimer’s disease.^{13,14} Not only does impaired sleep lead to the development of many illnesses, it is also associated with impaired healing and recovery,¹⁵⁻¹⁷ perhaps reflecting a further association with weakened immune system function.^{7,8} This type of problem – both predisposing to disease and impairing repair – is associated with accelerated health deficit accumulation, a problem for older adults, especially those who become acutely ill.^{18,19}

Sleep disturbance in older adults

Aging has been traditionally associated with changes to sleep quantity, quality, and timing. Roughly 30% of those 50 years and older may suffer from sleeping problems,²⁰⁻²² with more than 80% of those over 65 reporting some degree of disrupted sleep.²³ This disruption can be reflected in increased nighttime restlessness and daytime sleepiness. Most notable is the phase advance of the sleep–wake cycle relative to

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external time: many older people tend to go to bed earlier and awaken much sooner than younger adults.²⁴ The amplitude of the sleep–wake rhythm is reduced: older people tend to show less intense activity during their active phase and less sleep during their rest phase.²⁵ Total sleep time, however, appears to decrease only slightly or remain stable in healthy aging, with those 60 years and over sleeping an average of 6.5–7 hours a day.^{26,27}

Although aging itself does not always bring about changes in sleep quantity, it does cause distinct changes to sleep architecture.²⁸ Sleep tends to become shallower, with a greater percentage of the night being spent in the lighter sleep stages (1 and 2); electroencephalogram (EEG) recorded during stage 2 sleep contains fewer sleep spindles and smaller amplitude K complexes than it does in younger adults. One of the most profound changes is a decrease in the percentage of time spent in slow-wave sleep (stage 3), as characterized by a reduction in the number and amplitude of delta waves.²⁹ A meta-analysis of 65 studies³⁰ showed that in adults, there is a gradual reduction in the percentage of slow-wave sleep, rapid eye movement (REM) sleep latency, and sleep efficiency (time spent sleeping while in bed), and an increase in the percentage of stage 1 and 2, and wake after sleep onset, up to ~60 years; after which only sleep efficiency continues to decrease. Despite the many reports that REM sleep decreases with age,³⁰ when mental or physical illness are controlled for and various sleep characteristics are measured using polysomnography (PSG) or actigraphy (ie, sleep latency, sleep efficiency, total sleep time, REM sleep latency, wake after sleep onset, etc), the percentage of REM sleep appears to remain relatively stable in old age.³⁰

The decreased ability to maintain sleep once initiated, most often linked to some comorbid health condition, appears to be a major factor contributing to the increase in age-associated sleep complaints.^{28,31,32} Insomnia, which is typically defined as self-reported difficulty falling or staying asleep, accompanied by daytime sleepiness, is quite common in older people. Despite the characteristic changes in sleep parameters discussed above, difficulty sleeping might not be an inevitable part of healthy aging, but rather a consequence of other changes that accompany aging. There is an increase in the prevalence of a number of primary sleep disorders with aging. For example, obstructive sleep apnea increases in frequency with age, with prevalence rates as high as 62% in those over 60 years of age.³³ Periodic limb movements, which can severely disrupt sleep continuity, and restless legs syndrome, which can delay sleep onset, are also more common in older people. REM sleep behavior disorder

(involuntary, sometimes violent, movements during REM sleep, due to loss of muscle atonia) is also more common in older individuals. Interestingly, symptoms of this disorder appear to be present years prior to the diagnosis of Parkinson's disease; up to half of cases of REM sleep behavior disorder are later diagnosed with Parkinson's disease.³⁴

In addition, medical or psychiatric conditions may occur in aged individuals that disturb sleep indirectly (eg, prostatitis, loss of bladder elasticity, gastrointestinal disorders, chronic pain syndromes, and depression).²⁸ Drug treatments for some conditions that increase in frequency with aging can also disrupt sleep eg, diuretics for patients with hypertension, or antidepressants, especially those said to be “activating”.

The increase in sleep disorders and disturbance resulting from associated illnesses or medications may contribute to the degree of sleep disruption experienced by older people. Extensive health assessment can screen out nearly all sleep complaints and disorders in an older population,³⁵ providing further support for the link between illness and sleep abnormalities, rather than these disturbances being due to the aging process. Nevertheless, roughly 10% to 16% of community-dwelling adults over 65 have been noted to report chronic (primary) insomnia in the absence of an obvious precipitant.^{36,37} Age-associated changes in circadian organization, a decline in health due to aging, and hyperarousal from abnormalities to the hypothalamic-pituitary-adrenal axis appear to be contributing factors.^{38,39} Other biologically associated causes, such as conditions like “insomnia with short sleep duration”, may play a role as well.⁴⁰

The timing of sleep and wakefulness is influenced by the interaction between homeostatic sleep propensity and circadian processes, such that the circadian drive for wakefulness during the daytime opposes the gradual buildup of pressure for sleep as waking is sustained. Similarly, the circadian drive for sleep acts in opposition to the declining homeostatic need for sleep during the late part of a night's sleep.^{41–43} The changes observed during aging reflect a decline in the amplitude of signals from the circadian pacemaker to the sleep–wake regulatory regions.^{44–46} For example, one of the most robust circadian clock-controlled rhythms that becomes impaired with age is that of melatonin, a sleep-promoting hormone.^{47,48} The role of melatonin in the aging process is not well understood. Even so, nightly melatonin supplementation, alone or combined with magnesium (which also improves measures of insomnia),⁴⁹ has been shown to improve sleep disturbance in older adults^{50–52} as well as to diminish symptoms of REM sleep

behavior disorder.⁵³ These findings suggest a potential therapeutic role for melatonin in treating sleep disturbance symptoms in older individuals.

With age also comes an increased risk of neurodegenerative disease, the emergence of which often includes a lengthy prodromal period that can include impaired sleep. For example, sleep disturbances and alterations to the sleep–wake cycle have been observed prior to the onset of, not just motor symptoms of Parkinson’s disease but notably, other symptoms of Alzheimer’s disease^{54,55} and Lewy body dementia,⁵⁶ as well as being common throughout the course of frontotemporal dementia.⁵⁷ This makes it much more difficult to distinguish between normal age-related changes to sleep and changes that are due to an underlying degenerative process. Thus, interpreting sleep disturbances in a “healthy” younger-old population (ie, age 65–80) must be done with caution since these symptoms may be prodromal for the development of neurodegenerative diseases or other illnesses that may not be diagnosed until years later. For example, it remains unclear whether sleep impairment at this stage contributes to an increased risk of neurocognitive disorders later on in older hospitalized patients (eg, delirium).

Methods for the review

The aim of the present review was to provide a brief, yet comprehensive, overview of current data examining sleep characteristics (ie, quantity, quality, and circadian changes) in samples that included patients 80 years or older, who were admitted to the intensive care unit (ICU). The PubMed database was searched using the following key terms: “sleep”, “intensive care unit”, “ICU”, “80 years”, “older”, “elderly”, and “senior”. Excluding reviews, only those studies from the past 10 years that explicitly stated that individuals 80 years and older were included in their sample were considered. The search resulted in 19 studies that met our criteria (Table 1). Relevant studies referenced within these publications that met our criteria but that were older than 10 years were also included in our summary of findings.

Methods for studying sleep in the ICU

Sleep can be characterized in terms of: quantity (total sleep time and time spent in each stage); quality (wake after sleep onset, EEG patterns, and stage changes); and the circadian distribution (the pattern over a 24 hour cycle). To date, PSG remains the best method for assessing sleep, and although it may be time consuming to set up and may be uncomfortable

to wear for critically ill patients, it is the most reliable measure. Accurate recording relies on several measures, including at least three EEG signals, two electrooculography signals, and an electromyography signal from the submental muscle. Additional measures are typically recorded and may include oral and/or nasal airflow, abdominal movements, electrocardiogram, and pulse oximetry.⁵⁸ Even so, PSG recordings are not always possible in a critically ill patient, for reasons such as physical limitations and abnormal EEG patterns, including epileptogenic activity, altered consciousness, or various metabolic changes (eg, sepsis, intoxication, or medications).⁵⁹

When PSG is not feasible, several other methods may be employed. The easiest is subjective evaluation of changes in sleep and wake times by nursing staff and/or the patient. Sleep forms are easy to administer and very inexpensive. Even so, nurses have been shown to overestimate sleep time⁶⁰ and may fail to detect changes in patterns. This method also does not provide information about alterations in sleep architecture and may not be possible in all patients, particularly those with altered consciousness. For these individuals, the actigraphy method may be more applicable. Actigraphy involves the use of a wristwatch-like device that is placed on the patient’s wrist or ankle and records movements as an indicator of sleep or wakefulness. This is useful in many circumstances but often less so in ICU patients who typically have limited mobility, which may bias results. Actigraphy has also been shown to be a valid alternative for sleep assessment and an indicator of underlying sleep architecture.⁶¹ Finally, when EEG recording is possible from the frontal electrodes, the bispectral index may provide some information regarding depth of anesthesia (sedation), but it does not give any information about sleep architecture, and data collection is often inconsistent.⁶²

Sleep in the ICU

The ICU provides constant close monitoring of critically ill individuals who are experiencing a serious or life-threatening illness or injury. Sleep disturbance is common in ICU patients, with more than 60% of patients reporting having poor sleep or being sleep-deprived, when questioned prior to discharge.^{63,64} As assessed using 24-hour polysomnographic recordings, abnormal sleep–wake rhythms, sleep fragmentation, and shortened or absent REM and slow-wave sleep (important restorative components) are prominent features of those in the ICU.^{60,65–67} Sleep disruption in the ICU is recognized as impairing recovery and even contributing to mortality.^{68,69}

Table 1 Studies examining sleep in the intensive care unit that have included individuals 80 years and older

| Study | Sample age range | Sleep measures | Major findings |
|------------------------------------|------------------|---|---|
| Whitcomb et al ⁹⁹ | 68–83 | Wireless sleep monitor | Sedation and lack of REM sleep increased symptoms of delirium |
| Roche-Campo et al ¹⁰⁰ | 25–86 | PSG | Sleep quality higher during mechanical ventilation |
| Chang et al ¹⁰¹ | 65–86 | Recorded interviews (narratives) | Continuous sleep disrupted due to constant noise (eg, equipment, staff) |
| Chen et al ¹⁰² | 53–90 | PSG; actigraphy; nurse observations; Stanford Sleepiness Scale | Valerian, acupuncture increased sleep time, decreased wake frequency, decreased sleepiness |
| Drouot et al ⁵⁸ | 58–85 | PSG | Decreased REM sleep, slow EEG activity, impaired EEG reactivity during wakefulness |
| Savi et al ¹⁰³ | 35–80 | Nottingham Health Profile self-report questionnaire | Inspiratory muscle strength improved sleep quality |
| Zeilani and Seymour ¹⁰⁴ | 19–82 | Recorded interviews (narratives) | Pain was a contributing factor to sleep disturbance |
| Roche Campo et al ¹⁰⁵ | 72–85 | PSG | Noninvasive ventilation failure results in poorer sleep quality, less REM sleep, and greater circadian disruption |
| Kelly and McKinley ¹⁰⁶ | 19–84 | SF-36 | Interrupted sleep while in the ICU may be due to frequent interventions, uncomfortable beds or noise from machinery, conversations or other patients; survivors perceived good health despite disturbed sleep during recovery |
| Beecroft et al ¹⁰⁷ | 55–80 | PSG; actigraphy; nurse assessment | Decreased total sleep time and sleep efficiency, high frequency of awakenings; elevated stage 1 and decreased REM sleep; highly fragmented sleep |
| Bourne et al ¹⁰⁸ | 46–82 | Bispectral index; actigraphy; nurse assessment; patient self-report (Richards Campbell Sleep Questionnaire) | Melatonin increased nocturnal sleep by 1 hour |
| Cabello et al ¹⁰⁹ | 47–85 | PSG | Mechanical ventilation was associated with short REM sleep and increased sleep architecture fragmentation |
| Friese et al ¹¹⁰ | 20–83 | PSG | Average total sleep time was 8.23 hours; 6.2 hours of awakenings; reduced stages 3 and 4, and REM |
| Hweidi ¹¹¹ | 35–80 | Intensive Care Environmental Stressor Scale | Not being able to sleep was perceived as a primary stressor |
| Toublanc et al ¹¹² | 42–81 | PSG | Assist-control ventilation was associated with increased stages 1 and 2, and reduced wakefulness during first half of night; increased stages 3 and 4 during the second half of night |
| Hellgren and Ståhle ¹¹³ | 35–85 | SF-36 | No change |
| Olofsson et al ⁸⁰ | 52–83 | Melatonin secretion; nurse assessment (Sedation-Agitation Scale); bispectral index | Circadian rhythm of melatonin was abolished during deep sedation and mechanical ventilation |
| Tamburri et al ¹¹⁴ | 48–84 | Nurse activity checklist | High frequency of nocturnal care leaves few opportunities for uninterrupted sleep |
| Frisk et al ⁷⁷ | 41–88 | Melatonin secretion | Mechanical ventilation was association with decreased melatonin secretion |
| Frisk and Nordström ⁷⁶ | 19–85 | Nurse and patient questionnaire (Richards Campbell Sleep Questionnaire); patient interview | Hypnotics/sedatives results in poorer sleep scores; No difference between nurse and patient reports |
| Freedman et al ⁶⁵ | 20–83 | PSG | Environmental noise is partly responsible for qualitative reports of sleep disruption |
| Freedman et al ⁶³ | 19–86 | Self-report questionnaire | Poor sleep quality and daytime sleepiness is commonly reported in ICU settings |

Abbreviations: EEG, electroencephalogram; ICU, intensive care unit; PSG, polysomnography; REM, rapid eye movement; SF-36, self-report 36-item short-form health survey.

Various factors can influence sleep in the ICU.^{59,70–73} Despite the link between sleep and recovery from illness, the ICU can be a noisy and chaotic environment, which can have a significant negative impact on sleep; however, less than 30%

of awakenings in the ICU are reportedly due to environmental noise.^{65,74} Sleep disturbance in the ICU appears to be due to a combination of environmental factors, including noise, light exposure at night (which can suppress melatonin),

room temperature, routines of caretaking staff, and the impacts of mechanical ventilation, along with factors such as medications that may disrupt or promote sleep.⁷⁵

In addition to these environmental factors, endogenous mechanisms related to the illness itself, such as immune system responses to illness and pain or discomfort associated with the illness or with treatment interventions,⁷⁶ may disrupt sleep in patients whose sleep-regulatory and circadian systems may already be compromised. Altered circadian patterns of melatonin or virtually nonexistent secretion have also been noted in ICU patients.^{77,78} This abnormality is associated with mood and sleep disorders that are observed in elderly hospitalized patients⁷⁹ and may contribute to slower recovery in the critically ill.⁸⁰ Melatonin supplementation may serve as a promising new way to manage sleep disruption and delirium in the ICU; however, the research in this area is sparse.⁸¹ It is important for the critically ill to receive sufficient sleep as well as good sleep quality. Good quality sleep can contribute, along with other mechanisms, to more efficient and timely recovery and prevent possible negative outcomes.^{59,82,83}

Poor sleep can contribute to the onset of delirium, which occurs in up to 80% of ICU patients.⁸⁴ Delirium is characterized as a transient state of confusion and disorientation with fluctuating intensity, often accompanied by cognitive impairment. Delirium is a strong predictor of longer ICU length of stay, mechanical ventilation use, and even mortality.⁸⁵ Sleep deprivation can result in delirium-like symptoms, such as inattention and fluctuations in mental capacity; however, it is still unclear whether sleep disruption in the ICU is a cause, consequence, or comorbidity of delirium. That said, sleep disturbance appears to be a potential risk factor by interacting with various neurobiological systems that are involved in delirium.^{86,87}

Sleep in ICU patients aged ≥ 80 years

Increasing age is often accompanied by an increased risk of adverse health outcomes. This is particularly true of those ≥ 80 years, who exhibit a higher prevalence of illness and ICU admission compared with younger adults.^{88,89} With this comes a higher level of frailty or an increased vulnerability to poor outcomes, due to the accumulation of age-associated declines in the physiological reserve of multiple systems.^{90,91} Despite the importance of sleep to good health, the relationship between frailty and sleep disturbance has been sparsely studied^{92,93} and primarily among community-dwelling older adults.^{14,94-97} One recent study demonstrated

that nonfrail men 65 years and older (mean 75.7 years) who exhibited poor subjective sleep quality, increased nighttime waking, and greater nighttime hypoxemia were at high risk for showing increased frailty levels approximately 3 years later.⁹⁶ In the same sample, men who exhibited excessive daytime sleepiness, frequent nighttime awakenings, and sleep apnea were also at a greater risk for mortality.⁹⁶ Even so, overall health status, independent of daytime sleepiness and sleep disturbance, appears to be a stronger determinant when assessing risk of death.^{14,98}

How age itself impacts sleep in ICU patients is not yet clear. First, many studies that have examined sleep in the ICU do not report the age range of their sample. Since sleep characteristics and recovery processes can vary over the course of the lifespan, the extent to which sleep disturbance affects recovery in elderly ICU patients remains unclear, as does the nature of the sleep disturbance, particularly in the oldest of old (≥ 80 years). Second, even in those studies that do report age, there is often a wide age range (eg, 19–88 years).^{76,80,99-114} Third, the few studies that have examined the relationship between age and sleep in older adults in the ICU have failed to find an association between increasing age and sleep quality,^{63,65} even when analyses were stratified into young-old (< 75 years) and older-old (> 75 years).⁷⁶ This observation might reflect the fact that sleep parameters change only modestly in people over age 60 years, so sleep processes might be similarly affected by the ICU environment across this age range. The impact that age has on sleep in this population, especially with regards to health outcomes, is unknown because so few studies have examined this issue. In addition, other than Freedman et al⁶³ who excluded those with a history of dementia, other studies that included those ≥ 80 years did not take into account the potential influence of underlying causes, such as neurodegenerative disease.

Sleep disturbance and insomnia are generally quite prevalent in older hospitalized patients,¹¹⁵ which is reflected in the high rate of sedative-hypnotic drug prescriptions given to this population. Up to 41% and 96% of older patients in general and surgical wards, respectively, receive such prescriptions.^{116,117} These drugs tend to have greater negative effects in older individuals¹¹⁸ and might interact with other commonly prescribed medications (eg, those for blood pressure, cholesterol, and dementia), as well as increase the risk of falls, delirium, and rebound insomnia. Often, the small benefit that sedative-hypnotics have in this population does not justify the increased risk of adverse health outcomes,¹¹⁹ even following ICU admittance.⁸⁵

Taken together, these findings suggest that sleep disturbance might have prognostic utility in predicting future increases in frailty and a decline in health; however, the nature of this utility has not been examined – definitely not in ICU patients. One potential area, discussed above, that deserves further exploration is the role of melatonin. It is not possible to make recommendations at this time for the clinical use of melatonin in the ICU, due to the lack of well-designed randomized, controlled trials that take into account the effects of aging and other physical or psychiatric conditions; this is especially needed in those ≥ 80 years, who are often excluded from clinical trials. The interplay between sleep, circadian rhythms, frailty, and health outcomes of the critically ill oldest of old in the ICU remains unclear. It is also uncertain whether reducing sleep disturbance (eg, possibly by restoring normal nocturnal melatonin levels) in seriously ill patients can have a beneficial impact on their health outcomes. These questions should take precedence in our attempt to understand the reasons behind declining health in critically ill, hospitalized older individuals, and how it can be prevented.

Conclusion

Despite our increasing understanding of how hospitalization affects the sleep patterns of patients, there is still little known about the unique impact that critical care has on these parameters in the most frail and oldest of old. More work is required to determine whether and how these disturbances influence health outcomes, such as cognitive decline and mortality, of the seriously ill elderly. It is also crucial to understand how each patient's level of frailty interacts with these disturbances. For example, even a mild degree of impairment can lead to significant health decline in one individual but not in another with similar impairment. Does sleep disturbance contribute to, or determine, such outcomes?

Recognizing which aspects of health are associated with adverse outcomes can create better diagnostic measures that will capture these risk patterns. Greater awareness of these risks amongst health care professionals might decrease the chances of adverse outcomes in those admitted to the ICU; awareness may also guide more appropriate emergency treatment for those who are critically ill, which may include not undertaking certain medical treatments that will put the patient at risk of further decline or death. Ultimately, studies should be undertaken to establish potential intervention strategies to delay or prevent a decline in health status following ICU admission; these studies should include rigorous trials of interventions to improve sleep, as a potentially important

factor that can affect healing and recovery.⁵⁹ Such studies should also specifically include older adults, who commonly experience health declines in the ICU with a high rate of adverse outcomes but who, even so, often are excluded from clinical trials.^{18,120}

Disclosure

The authors report no conflicts of interest in this work.

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