Daytime-to-Nighttime Sleep Ratios and Cognitive Impairment in Older Intensive Care Unit Survivors

By Maya N. Elías, PhD, RN, Cindy L. Munro, PhD, ANP-BC, and Zhan Liang, PhD, RN

Background Sleep duration and proportion of daytime versus nighttime sleep may affect cognitive function in older patients in the transition out of the intensive care unit.
Objective To explore the relationship between the daytime-to-nighttime sleep ratio and cognitive impairment in older intensive care unit survivors.
Methods The study enrolled 30 older adults within 24 to 48 hours after intensive care unit discharge. All participants were functionally independent before admission and underwent mechanical ventilation in the intensive care unit. Actigraphy was used to estimate daytime (6 AM to 9:59 PM) and nighttime (10 PM to 5:59 AM) total sleep duration. Daytime-to-nighttime sleep ratios were calculated by dividing the proportion of daytime sleep by the proportion of nighttime sleep. The National Institutes of Health Toolbox Cognition Battery Dimensional Change Card Sort Test (DCCST) was used to assess cognition. Associations between sleep and cognition were explored using multivariate regression after adjusting for covariates.
Results The mean (SD) daytime sleep duration was 7.55 (4.30) hours (range, 0.16-14.21 hours), and the mean (SD) nighttime sleep duration was 4.99 (1.95) hours (range, 0.36-7.21 hours). The mean (SD) daytime-to-nighttime sleep ratio was 0.71 (0.30) (range, 0.03-1.10). Greater daytime sleep duration ($\beta = -0.351$, $P = .008$) and higher daytime-to-nighttime sleep ratios ($\beta = -0.373$, $P = .008$) were negatively associated with DCCST scores.
Conclusions The daytime-to-nighttime sleep ratio was abnormally high in the study population, revealing an altered sleep/wake cycle. Higher daytime-to-nighttime sleep ratios were associated with worse cognition, suggesting that proportionally greater daytime sleep may predict cognitive impairment. (*American Journal of Critical Care.* 2021;30:e40-e47)

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Even more than 1 year after critical illness, about 25% of adult intensive care unit (ICU) survivors experience post-ICU cognitive impairment comparable in severity to that of mild Alzheimer disease, and about 33% have cognitive impairment comparable to that associated with moderate traumatic brain injury.[1] Critically ill older adults, especially those who have undergone mechanical ventilation, are at highest risk for post-ICU cognitive impairment.[2]

Older adults require adequate sleep throughout recovery from critical illness.[3] Altered sleep distribution throughout the 24-hour sleep/wake cycle is common in ICU patients: more than 50% of total sleep time in the ICU occurs during the daytime,[4] and such sleep is highly fragmented, particularly among patients receiving mechanical ventilation.[5] The extent to which these sleep alterations persist after ICU and hospital discharge remains largely unknown.

Post-ICU cognitive impairment is a component of post-ICU syndrome,[6] which contributes to geriatric syndromes. At the time of hospital discharge, up to 90% of older ICU survivors have at least 1 geriatric syndrome,[7] which may include cognitive decline.[8,9] Significant advancements in critical care have improved mortality rates among hospitalized older ICU survivors. In fact, adults aged 65 and older who have undergone mechanical ventilation during their ICU stay are now more likely to survive until hospital discharge, but with greater comorbidity and disability.[10]

Pre-ICU or premorbid risk factors for post-ICU cognitive impairment may include age; sex; medical, neurological, or psychiatric history; preexisting cognitive impairment; apolipoprotein E genotype, and/or drug and alcohol abuse.[11] Intensive care unit–related risk factors for post-ICU cognitive impairment may include mechanical ventilation, sedation and analgesic use, hypotension and hypoxemia, glucose dysregulation, sepsis, acute renal failure, neurological dysfunction, and metabolic abnormalities.[12,13] Many of these pre-ICU and ICU-related risk factors for post-ICU cognitive impairment also overlap with risk factors for post-ICU sleep alterations (ie, mechanical ventilation, sedation and analgesic use, cardiovascular and respiratory medications, sepsis and infection, stress and anxiety, preexisting illnesses, and severity of illness).[4,14] Post-ICU cognitive impairment[15] and sleep disturbances[16,17] are prevalent among ICU survivors even after hospital discharge.

To our knowledge, researchers have not yet examined the association between objective measures of sleep and cognitive impairment in hospitalized older ICU survivors who received mechanical ventilation while in the ICU. Rather, research on sleep (using objective measures, such as actigraphy or polysomnography) and cognition in older adults has focused on relatively healthy, community-dwelling older adults[18-23] or older adults discharged from an inpatient postacute rehabilitation facility.[24]

The aims of the present study were (1) to examine the relationship between sleep duration and cognitive impairment, (2) to calculate the daytime-to-nighttime sleep ratio in study participants, and (3) to explore the relationship between this daytime-to-nighttime sleep ratio and cognitive impairment in hospitalized older ICU survivors. We hypothesized that, because sleep alterations contribute to cognitive decline even in healthy aging,[25,26] this relationship may be exacerbated by critical illness, with a higher post-ICU daytime-to-nighttime sleep ratio being negatively associated with cognitive impairment.

> Cognitive impairment and sleep disturbances are prevalent among older ICU survivors.

Methods

Study Design and Ethical Considerations

This small, exploratory study used a cross-sectional design. The study was approved by the university institutional review boards, and all participants provided written informed consent in English before enrollment, per the study protocol.

Sample and Setting

We enrolled 30 English-speaking hospitalized older ICU survivors (aged ≥65 years) who were functionally independent before hospital admission, had no preexisting diagnosis of dementia, and required mechanical ventilation (≥12 hours) while in the ICU.

About the Authors
Maya N. Elías is a postdoctoral research fellow, **Cindy L. Munro** is dean and a professor, and **Zhan Liang** is an assistant professor, School of Nursing and Health Studies, University of Miami, Coral Gables, Florida.

Corresponding author: Maya N. Elías, PhD, RN, 5030 Brunson Dr, Ste 423, Coral Gables, FL 33146 (email: mxe513@miami.edu).

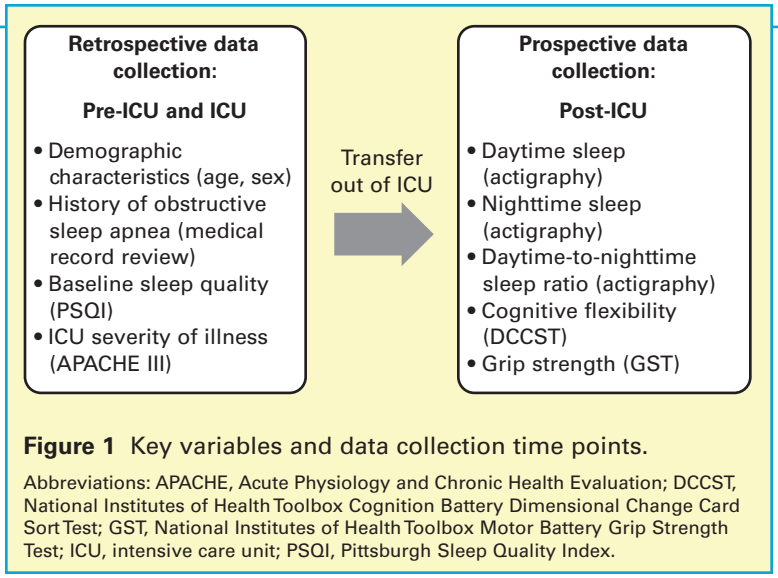

Figure 1 Key variables and data collection time points.

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; DCCST, National Institutes of Health Toolbox Cognition Battery Dimensional Change Card Sort Test; GST, National Institutes of Health Toolbox Motor Battery Grip Strength Test; ICU, intensive care unit; PSQI, Pittsburgh Sleep Quality Index.

We recruited patients from all 12 medical-surgical floors of a level I trauma hospital, regardless of admission diagnosis or type of ICU, within 24 to 48 hours after ICU discharge. Participants were selected through convenience sampling between November 2017 and January 2018. The time window of within 24 to 48 hours of transfer out of the ICU was chosen to capture the early post-ICU period.

To be included in the study, participants had to be previously community-dwelling adults (ie, admitted from home) aged 65 years or older and able to speak English to provide informed consent and participate in data collection. In addition, participants had to have been functionally independent before hospital admission. The Katz Index of Independence in Activities of Daily Living, a subjective measure of physical function, was used to assess the participant's baseline functional ability (ie, before hospital admission) to independently perform 6 activities of daily living: bathing, dressing, toileting, transferring, continence, and feeding.[27] The Katz Index has demonstrated high reliability, with Cronbach α coefficients ranging from 0.87 to 0.94.[28] Potential participants who scored less than 6 on the Katz Index (range, 0-6, with 6 indicating functional independence without any supervision or assistance required) were deemed ineligible for the study. Participants were asked to retrospectively comment on their baseline ability to perform each of these activities of daily living independently 2 weeks before hospital admission.[29] Exclusion criteria were imminent death, active palliative care or hospice orders, and history or suspicion of preexisting dementia on medical record review.

We then calculated the "daytime-to-nighttime sleep ratio" by dividing the proportion of daytime sleep by the proportion of nighttime sleep.

Measures and Procedures

The variables and measures included in our analyses, as well as data collection time points, are summarized in Figure 1.

Sleep Duration. Wrist actigraphy (Actiwatch Spectrum [Philips]) was used to collect data on total daytime sleep duration and nighttime sleep duration consecutively throughout a 2-night/1-day observation period, beginning at the time of study enrollment. Actigraphy has been used to measure sleep/rest versus activity in hospitalized patients,[30-32] in ICU patients,[33] and among ICU survivors after hospital discharge.[16] Acceleration counts were collected in 15-second epochs. We defined "daytime sleep duration" as the duration of sleep between 6 AM and 9:59 PM during 1 daytime observation period. We defined "nighttime sleep duration" as the mean duration of sleep of the 2 consecutive nighttime periods between 10 PM and 5:59 AM. We then defined "24-hour sleep duration" as the sum of daytime sleep duration and the mean nighttime sleep duration for analyses. Daytime and nighttime hours were chosen on the basis of unit routines at the hospital site; for example, on most units, checks of vital signs were typically scheduled for 6 AM, 10 AM, 2 PM, 6 PM, 10 PM, and 2 AM.

Daytime-to-Nighttime Sleep Ratio. Sleep efficiency was defined as the sleep duration divided by the total number of hours spent in bed.[33] We analyzed daytime sleep efficiency (between 6 AM and 9:59 PM, for a single 16-hour daytime period) and nighttime sleep efficiency (between 10 PM and 5:59 AM, averaged over 2 consecutive 8-hour nighttime periods) using wrist actigraphy. We then calculated the "daytime-to-nighttime sleep ratio" by dividing the proportion of daytime sleep by the proportion of nighttime sleep. As an example, a healthy older adult who does not sleep or nap during the 16-hour daytime period but sleeps for 6 out of the 8 hours during the nighttime period would have a ratio of 0 ([0/16]/[6/8]) (Figure 2).

Cognition/Executive Function. The National Institutes of Health (NIH) Toolbox Cognition Battery[36] Dimensional Change Card Sort Test (DCCST) was used to assess cognitive flexibility. Cognitive flexibility is a subdomain of executive function. Specifically, cognitive flexibility is the set-shifting component of executive function and consists of the ability to shift responses based on rules or contingencies. The first author (M.N.E.), who attended a live 2-day training

workshop on the NIH Toolbox measures, administered all 30 DCCST assessments. The DCCST assessments were completed on the day after the participant's enrollment in the study, during the daytime (ie, the second day of sleep observation). Assessments were completed at the bedside: before conducting the DCCST, the researcher approached the assigned nurse and requested an "appointment" for an uninterrupted period of about 5 to 10 minutes to complete the assessment. The DCCST has demonstrated good reliability (intraclass correlation coefficients ranging from 0.82 to 0.92) and good construct validity (convergent validity coefficient of –0.52).[36,37] Fully corrected *T* scores (adjusted for age, sex, race/ethnicity, and level of education; range, 0-100) on the DCCST were used for analyses.

Covariates. Age, sex, history of obstructive sleep apnea (OSA), and severity of illness score on ICU admission (Acute Physiology and Chronic Health Evaluation [APACHE] III[38]) were collected via medical record review. We assessed baseline sleep quality before hospital admission using the Pittsburgh Sleep Quality Index (PSQI).[39] The PSQI holds internal consistency, demonstrates high reliability (Cronbach $\alpha = 0.83$) for its 7 components, and has been validated in both older men[40] and older women.[41] Participants answered questions on the PSQI at the time of enrollment on the basis of how they slept at home, and higher PSQI global scores indicated worse sleep quality (range, 0-21). We assessed grip strength at time of enrollment using the NIH Toolbox Motor Battery Grip Strength Test (GST)[42] of handgrip dynamometry, because motor impairment is a component of post-ICU syndrome,[6] and the GST fully corrected *T* score was used for analyses. The test-retest reliability of grip strength measured by the GST was good to excellent (intraclass correlation coefficients ranging from 0.88 to 0.98).[42]

Statistical Analyses

Data were analyzed with IBM SPSS Statistics, version 26. Pearson correlation coefficients were used to examine bivariate correlations; covariates with correlation coefficients less than 0.20 were considered for inclusion in the models. Exploratory multivariate regression models were used to examine the cross-sectional associations between the independent variables (total daytime sleep duration, mean nighttime sleep duration, 24-hour sleep duration, and daytime-to-nighttime sleep ratio) and the dependent variable (fully corrected *T* score on the DCCST), after adjusting for the selected covariates. Model 1 adjusted for age, sex, history of OSA, and PSQI. Model 2 adjusted for age, sex, history of OSA, PSQI, APACHE III, and GST.

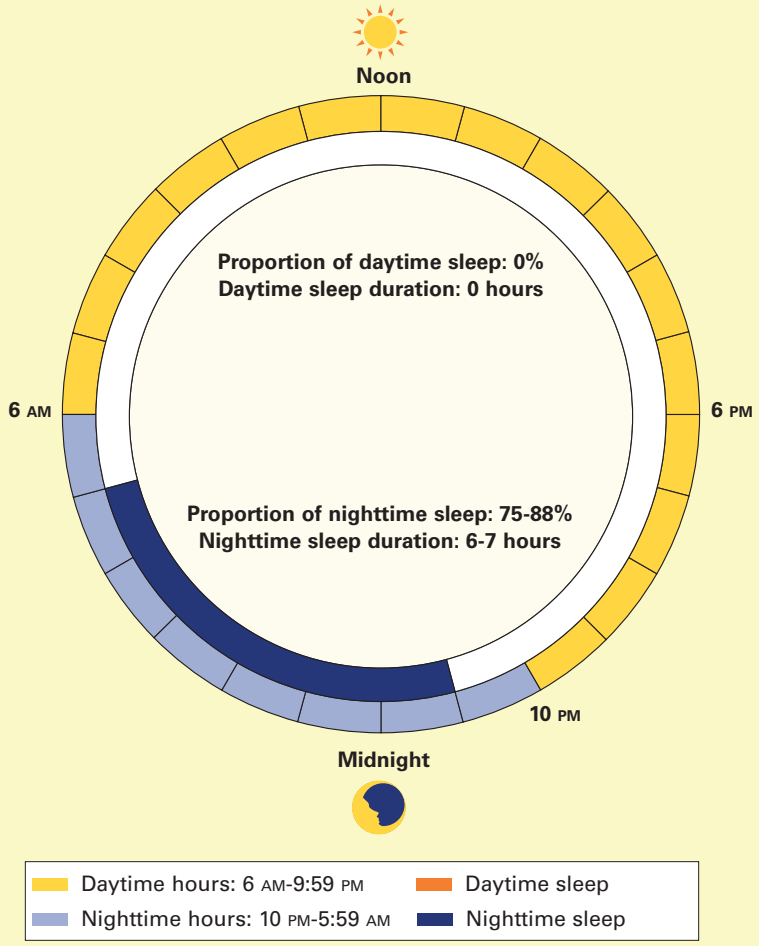

Figure 2 Example of typical proportions of daytime versus nighttime sleep for a healthy community-dwelling older adult. Healthy, active, community-dwelling older adults typically do not experience sleep disturbances[34]—rather, they sleep primarily during nighttime hours, and thus should not need to nap during the daytime because of excessive daytime sleepiness.[35] Therefore, their ratio of daytime sleep to nighttime sleep should be zero.

Results

Sample Characteristics

A total of 26 participants with complete data on all aforementioned measures were included in the final analyses. One participant was transferred back to the ICU after only 1 night of actigraphy, and 3 participants did not fully complete the DCCST. Of the 26 participants, the mean (SD) age was 70.62 (4.77) years, 10 (38%) were female, and 22 (85%) identified as White and non-Hispanic/Latino. On average, participants spent 5.43 (7.89) days receiving mechanical ventilation while in the ICU; the mean ICU length of stay was 12.46 (12.14) days. The mean APACHE III score was 96.19 (29.47) (range, 50-157),

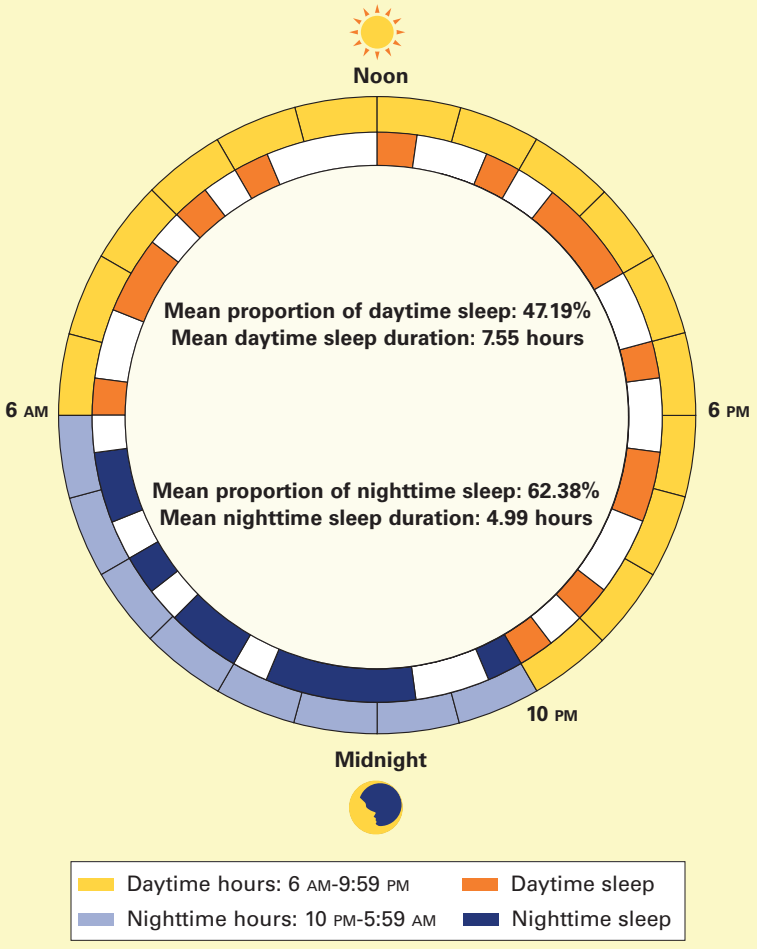

Figure 3 Example of the proportions of daytime versus nighttime sleep among older intensive care unit survivors in the study sample. This figure also reflects the care routines of the hospital setting, for example, unit routines for measuring vital signs (6 AM, 10 AM, 2 PM, 6 PM, 10 PM, 2 AM) and scheduled mealtimes (6:45 AM, 11 AM, 4:30 PM).

the mean PSQI score was 6.5 (2.7) (range, 1-12), and 15 participants (58%) had preexisting OSA. The mean fully corrected *T* score on the GST was 34.04 (13.31) (range, 5-59). A total of 12 participants (46%) received care in the medical ICU, 9 (35%) in the cardiovascular ICU, 2 (8%) in the surgical/trauma ICU, 2 (8%) in the surgical/transplant ICU, and 1 (4%) in the neurological/neurosurgical ICU.

Descriptive Analyses of Cognition and Sleep

The mean (SD) DCCST fully corrected *T* score was 38.81 (9.2) (range, 24-64), which is greater than 1 SD below the normative population DCCST scores of healthy, community-dwelling older adults.

Participants' mean (SD) nighttime sleep duration was 4.99 (1.95) hours (range, 0.36-7.21 hours) between the hours of 10 PM and 5:59 AM, whereas the mean daytime sleep duration was 7.55 (4.30) hours (range, 0.16-14.21 hours) between the hours of 6 AM and 9:59 PM. The mean 24-hour sleep duration was 12.48 (5.93) hours (range, 0.53-20.77 hours).

The mean (SD) daytime-to-nighttime sleep ratio was 0.71 (0.30) (range, 0.03-1.10). The ratios for 5 (19%) participants were greater than 1, indicating that these participants slept proportionally more during the day than at night. An example of the proportion of daytime versus nighttime sleep over a 24-hour period in these older ICU survivors is shown in Figure 3.

Exploratory Regression Models

Exploratory regression models revealed that greater daytime-to-nighttime sleep ratios were negatively associated with cognitive flexibility. All exploratory regression models are detailed in the Table.

Association Between Daytime Sleep and Cognition. The regression model (Model 1) exploring the relationship between daytime sleep duration and cognitive flexibility showed a statistically significant association ($R^2 = 0.748$, $P < .001$). Greater daytime sleep duration was negatively associated with DCCST scores ($\beta = -0.351$, $P = .008$) after adjusting for covariates. The unique variance for daytime sleep duration was 11.6%: greater daytime sleep duration was significantly associated with worse cognitive flexibility. An additional regression model with added covariates (Model 2) also supported this negative association between daytime sleep duration and cognitive flexibility.

Association Between Daytime-to-Nighttime Sleep Ratio and Cognition. The regression model (Model 1) exploring the relationship between the daytime-to-nighttime sleep ratio and cognitive flexibility also indicated a statistically significant association ($R^2 = 0.750$, $P < .001$). Higher daytime-to-nighttime sleep ratios were negatively associated with DCCST scores ($\beta = -0.373$, $P = .008$) after adjustment for covariates. The unique variance for daytime-to-nighttime sleep ratio was 12.2%: higher daytime-to-nighttime sleep ratios were significantly associated with worse cognitive flexibility. An additional regression model with added covariates (Model 2) also supported this negative association between daytime-to-nighttime sleep ratios and cognitive flexibility.

Discussion

Our study revealed that greater post-ICU daytime sleep duration was significantly associated with cognitive impairment, specifically in terms of cognitive flexibility, despite transition of care out of the

Table
Associations between sleep and cognitive flexibility (DCCST)

Sleep predictor variable	Model 1[a]				Model 2[b]			
	R^2; F	P[c]	β (95% CI)	P[c]	R^2; F	P[c]	β (95% CI)	P[c]
Daytime sleep[d]	0.748; $F_{5,19}=11.263$	<.001	−0.351 (−1.309 to −0.222)	.008	0.779; $F_{7,17}=8.545$	<.001	−0.286 (−1.214 to −0.035)	.04
Nighttime sleep[e]	0.639; $F_{5,20}=7.069$	.001	−0.181 (−2.259 to 0.554)	.22	0.697; $F_{7,18}=5.905$	.001	−0.144 (−2.149 to 0.788)	.34
24-hour sleep[f]	0.720; $F_{5,19}=9.780$	<.001	−0.308 (−0.905 to −0.070)	.02	0.761; $F_{7,17}=7.734$	<.001	−0.245 (−0.835 to 0.058)	.08
Daytime-to-nighttime sleep ratio[g]	0.750; $F_{5,18}=10.825$	<.001	−0.373 (−19.907 to −3.391)	.008	0.799; $F_{7,16}=9.084$	<.001	−0.322 (−18.276 to −1.83)	.02

Abbreviations: β, standardized coefficients; DCCST, National Institutes of Health Toolbox Cognition Battery Dimensional Change Card Sort Test fully corrected T score (outcome variable for all associations with sleep predictor variables); R^2, regression coefficient of determination.

[a] Model 1: adjusted for age, sex, history of obstructive sleep apnea, and Pittsburgh Sleep Quality Index global score.
[b] Model 2: adjusted for age, sex, history of obstructive sleep apnea, Pittsburgh Sleep Quality Index global score, Acute Physiology and Chronic Health Evaluation III score, and National Institutes of Health Toolbox Motor Battery Grip Strength Test fully corrected T score.
[c] Significant at the $P<.05$ level.
[d] Daytime sleep: sleep duration in hours between 6 AM and 9:59 PM.
[e] Nighttime sleep: sleep duration in hours between 10 PM and 5:59 AM, averaged over 2 consecutive nights.
[f] 24-hour sleep: sum of daytime sleep duration and nighttime sleep duration.
[g] Daytime-to-nighttime sleep ratio: proportion of daytime sleep divided by proportion of nighttime sleep.

ICU. Moreover, the daytime-to-nighttime sleep ratio was abnormally high, indicating severe alterations of the sleep-wake cycle, with a proportionally large amount of post-ICU sleep occurring during the day. Alterations in the sleep-wake cycle are significantly influenced by aging; these changes can contribute to cognitive decline even in cases of healthy aging[25] and may be exacerbated by sudden critical illness. A healthy and active older adult typically does not experience sleep disturbances,[34] sleeping primarily during nighttime hours with short sleep latency and high sleep efficiency, and therefore should not need to nap during the daytime because of excessive daytime sleepiness (Figure 2).[35]

We found significant associations between greater daytime sleep duration and post-ICU cognitive impairment in a cohort of older ICU survivors. Other studies examining objectively measured sleep and cognition in older adults have focused on relatively healthy, community-dwelling older adults[18-23] or older adults discharged from an inpatient postacute rehabilitation facility.[24] Excessive daytime sleepiness has also been shown to be linked to cognitive decline in community-dwelling elderly people.[43] Yet these populations are not as clinically complex as our sample of older ICU survivors. Moreover, most of these studies did not report on a ratio of daytime-to-nighttime sleep or its possible link to cognition. One study (of community-dwelling older women) indicated an increased risk of cognitive impairment among older women who napped more than 2 hours daily.[20] Another study suggested that lower daytime sleep duration was associated with improvements in cognitive function among older men discharged from a Veterans Administration–affiliated, postacute rehabilitation facility.[24] The findings from these 2 studies particularly support the present study of hospitalized older ICU survivors, in which a higher daytime-to-nighttime sleep ratio was associated with worse executive function.

Our results suggest that a greater quantity of sleep may not necessarily translate to a better quality of sleep even after discharge from the ICU. There may be an "optimal dose" of sleep duration, and both short and long sleep durations may be associated with worse cognitive performance across subdomains of executive function among healthy, community-dwelling older adults.[44,45] Moreover, our results reveal that the sleep/wake cycle remains altered beyond ICU discharge and may still favor greater proportions of daytime sleep during hospitalization. Thus, we suggest that alterations of the sleep/wake cycle (ie, altered distribution of sleep between nighttime and daytime hours to favor greater daytime sleep) might exacerbate post-ICU cognitive impairment among older ICU survivors.

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older ICU survivors. Additional research is needed to clarify these relationships between sleep and cognition in ICU survivors.

Study Limitations

One limitation of this study is the lack of a pre-ICU cognitive assessment or baseline self-report, although participants with preexisting or suspected dementia were excluded from enrollment. Pre-ICU cognitive status may provide prognostic information about the likelihood of older adults maintaining independence after a critical illness.[46] Per our study protocol, we collected data (retrospective medical record review) at the time of study enrollment regarding documentation of ICU delirium by a provider (ie, physician, psychiatrist, nurse practitioner, or registered nurse). However, clinical documentation of ICU delirium in elderly ICU patients has been notoriously unreliable for use in research studies[47,48] and thus was not included as a covariate in our analyses. Actigraphy uses accelerometry and thus may overestimate sleep duration and sleep efficiency, yet actigraphy has been well validated compared with polysomnography.[49] The ease and low cost of its use renders actigraphy a feasible option, instead of polysomnography, for any study protocols designed to evaluate sleep in the ICU and beyond the ICU.[33] Finally, although our sample size was very modest, the preliminary results from these actigraphy data informed the design of a more robust, longitudinal cohort study using portable polysomnography (NIH award number F32NR018585) to examine post-ICU sleep and cognition.

Conclusion

Post-ICU cognitive impairment is part of post-ICU syndrome, and among older ICU survivors, altered sleep may be a considerable risk factor for the development of cognitive impairment.[6] Older adult ICU survivors experience long-term impairments in cognition that persist beyond the ICU and throughout transitions of care.[50,51] Executive function scores of people who survive critical illness are reported to be significantly lower than the population mean,[1] which our results also support. Executive function is a prerequisite for higher cognitive capacity and functional status among older adults.[52] Poor executive function is independently associated with institutionalization (discharge to a skilled nursing facility or long-term acute/subacute care) at hospital discharge.[53-55] Less than 25% of older adults who receive mechanical ventilation during hospitalization are discharged home.[56] In contrast, more than half of older ICU survivors who receive mechanical ventilation are discharged to a skilled nursing facility.[10] Sleep promotion should continue after ICU discharge, as sleep may be crucial for older adults' recovery beyond the ICU; thus, health care providers in post-ICU units should promote daytime activity and mobility while attempting to optimize nighttime sleep.[57] Ultimately, we propose that improving post-ICU sleep may help prevent or mitigate post-ICU cognitive decline and thus may reduce symptom burden and health care costs among older ICU survivors.

FINANCIAL DISCLOSURES
None reported.

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