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Short sleep duration following hospital evaluation for acute coronary syndrome is associated with increased risk of 6-month readmission

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Abstract

Objective: Hospital readmission following acute coronary syndrome (ACS) is associated with worsened patient outcomes and financial burden. Short sleep duration is a risk factor for cardiovascular events, and may therefore represent a behavioral factor that increases risk of adverse post-hospitalization outcomes. This study examined whether short sleep duration in the month after hospital evaluation for ACS is associated with 6-month all-cause emergency department (ED) and hospital readmission.

Methods: The current analyses entail a secondary analysis of a larger prospective observational cohort study. Sleep duration during the month following hospital evaluation for ACS was assessed subjectively and dichotomized as short (<6 hours) or not short (≥ 6 hours). A Cox proportional hazards model was used to assess the association between short sleep duration during the month following ACS hospital evaluation and 6-month all-cause ED/hospital readmission.

Results: A total of 576 participants with complete data were included in analyses. Approximately 34% of participants reported short sleep duration during the month following ACS evaluation. Short sleep duration was significantly associated with 6-month all-cause ED/hospital readmission (HR=2.03; 95% CI: 1.12–3.66) in the model adjusted for age, sex, race/ethnicity, clinical severity, cardiac and renal markers, depression, acute stress, and including a sleep duration × ACS status interaction.

Conclusions: Short sleep duration following ACS hospital evaluation is prevalent, and is associated with increased risk of all-cause readmission within 6 months of discharge. Current findings suggest that short sleep duration is an important modifiable behavioral factor to consider following hospital evaluation for ACS.

Keywords

sleep; acute coronary syndrome; readmission

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Introduction

Over 30% of patients experiencing acute coronary syndrome (ACS; myocardial infarction or unstable angina) will have an emergency department (ED) or inpatient hospital readmission within 30 days of discharge, and over 60% will have a hospital visit within 1 year (1). Early post-ACS readmission is associated with worsened patient outcomes and financial burden (1). The identification of modifiable factors related to post-ACS readmission can therefore ultimately help inform preventive interventions.

Short sleep duration (typically defined as <6-7 hours per night) is an established risk factor for incident cardiovascular disease (CVD) risk (2). In addition, we have previously demonstrated in the Prescription Use, Lifestyle, Stress Evaluation (PULSE) study, that self-reported short sleep duration in the month after ACS hospitalization is also associated with a 50% increased risk of 1-year CVD recurrence or mortality (3). A recent study of approximately 13,000 patients with ACS found that individuals who report short sleep duration (<6 hours per night) within the month following the ACS event had a 29% higher risk of major coronary event (coronary heart disease death, myocardial infarction, or urgent coronary revascularization) over a ~3-year follow-up, compared to those who reported sleeping over 6 hours per night (4). These prior findings reinforce the relationship between short sleep duration and CVD following ACS. However, they did not examine the association between sleep duration following hospital evaluation for ACS and all-cause hospital or ED readmission, which is the research question in the current report.

Short sleep duration may contribute to rehospitalization risk by altering cardiometabolic processes (5-9). These include, but are not limited to: disrupting insulin signaling (5) and endothelial function (6), and increasing blood pressure (7, 10) and inflammation (8, 9). Aside from CVD, short sleep duration may also be hazardous by contributing to more general risks associated with fatigue, sleepiness, and attendant cognitive deficits (e.g. falls, missed medications).

Short sleep duration is common following ACS (3), and may be an important modifiable behavioral factor to consider following hospital evaluation for ACS. We therefore examined whether short sleep duration following hospital evaluation for ACS was associated with 6-month all-cause ED and hospital readmission.

Methods

Participants in the current analysis were patients with a diagnosis of probable ACS who were enrolled in the Reactions to Acute Care and Hospitalization (REACH) study. REACH is an observational cohort study examining how environmental (i.e. ED-related), psychosocial, and behavioral factors relate to adverse long-term health outcomes following hospital evaluation for ACS. Participants were enrolled during ED evaluation for ACS at New York-Presbyterian Hospital/Columbia University Medical Center, a large quaternary academic medical center serving a dense urban area in Northern Manhattan. Participants were eligible for inclusion in the REACH study if they were at least 18 years of age, were English- or Spanish speakers, and if they had chest pain and a suspected diagnosis of non-ST

segment elevation myocardial infarction or unstable angina during initial presentation in the ED. Exclusion criteria included being unable to complete assessments and follow-up, lack of reliable phone or email access, being deemed unable to comply with protocol (e.g. by self-selection, or because of cognitive impairment), those with a need for psychiatric intervention within 72 hours of enrollment, or those unlikely to be available for follow-up (e.g. prisoners, leaving the United States soon, life expectancy < 1 year). ACS events were defined according to American Heart Association/American College of Cardiology criteria as either acute myocardial infarction or unstable angina (11, 12). Participants were enrolled in the study during their ED evaluation and some were found to not be experiencing an ACS event. Verified ACS at the time of enrollment was therefore not an inclusion criterion, and accordingly, a large portion of the participants did not have ACS. After providing informed consent, participants underwent a brief interview and completed questionnaires. Follow-up assessments were conducted by telephone interview. Participants in the current report were enrolled in the study between November 2013 and February 2016. Prior work, focusing on acute stress (13), threat perception (14-18), posttraumatic stress disorder (19-24), and the ED environment (25, 26), within this cohort has been published. This is the first examination of sleep within this cohort.

Measures of interest in the current report were sleep duration and 6-month all-cause ED and hospital readmission. Sleep duration and the use of medications for sleep following discharge from ACS evaluation were assessed at 30-day follow-up with two questions based on the Pittsburgh Sleep Quality Index (PSQI), a widely used and validated self-report measure of typical sleep habits during the past month (27). Sleep duration was assessed with the following question: "During the past month, how many hours of actual sleep did you get at night?", and dichotomized as short (<6 hours) or not short (≥ 6 hours) (28). Exploratory analyses considered long sleep as >8 hours (29). Use of medication for sleep was assessed with the question "During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?" Responses included "Not during the past month", "Less than once per week", "Once or twice a week", and "Three or more times per week". ED/hospital readmission within 6 months of ACS evaluation was identified by contacting patients and by proactively searching electronic health records for all participants daily. All-cause ED or hospital readmission (not limited to cardiovascular events) were included. These included any ED visits and any unscheduled hospitalizations. All procedures were approved by the Institutional Review Board of Columbia University Irving Medical Center. All participants provided written informed consent.

A Cox proportional hazards model was used to assess the association between short sleep duration during the month following ACS evaluation and 6-month all-cause ED/hospital readmission, while adjusting for age, sex, race/ethnicity, clinical severity (Charlson comorbidity index, Global Registry of Acute Coronary Events [GRACE] score), ACS status (verified ACS event: yes or no), renal function (creatinine), cardiac marker (troponin I), depression, and stress at baseline. Depression was assessed with the Patient Health Questionnaire (PHQ-2) scale. Stress was assessed using the acute stress disorder symptom (ASDS) scale. The PHQ-2 scale consists of the first two items of the PHQ-9 scale, i.e., depressed mood and anhedonia (30). The PHQ-2 has good specificity and sensitivity for detecting depression and is comparable to the full PHQ-9 (30). The PHQ-2 was used here

since it does not include Item 3 of the PHQ-9 (“trouble falling asleep, staying asleep, or sleeping too much”). Fourteen items from the ASDS scale (total score range: 14-70) were used to evaluate participants’ reported acute stress disorder symptoms (i.e., early posttraumatic stress symptoms: re-experiencing and/or avoiding reminders of the trauma, hyperarousal) in response to the event that initially brought them to the ED (31). The analyses also included an interaction term for short sleep duration (yes/no) $\times$ verified ACS (yes/no). Time-to-event was calculated as the number of days between initial discharge and first ED or hospital readmission with right censoring at 180-days for those who experienced all-cause mortality or remained event-free. Participants who experienced an ED/hospital readmission prior to the 1-month sleep assessment were excluded from analyses. Analyses were conducted using SPSS Statistics for Windows, Version 24.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 576 participants with complete data were included. Of these, $n=198$ had verified ACS (34%) and $n=378$ did not have verified ACS (66%). Non-ACS diagnoses consisted of chest pain from a non-cardiac etiology ($n=328$, 87%; e.g., musculoskeletal pain, gastrointestinal disorder, anxiety-related disorder, drug intoxication, other unspecified cause) and non-ACS cardiac diagnoses ($n=50$, 13%; e.g., congestive heart failure, pericarditis, hypertensive urgency).

Approximately 34% of participants reported short sleep duration during the month following ACS evaluation (Table 1). Participants who reported short vs. not short sleep duration were more likely to be female ($p=0.005$) and black ($p=0.041$), and less likely to be white ($p=0.046$) (Table 1). No differences were seen in clinical severity (Charlson comorbidity index and GRACE-Risk score, $p=0.18$ and $p=0.98$, respectively) in individuals reporting short vs. not short sleep. Depression scores were significantly higher in participants reporting short vs. not short sleep duration (PHQ-2 scores: 1.85 ± 2.04 vs. 1.37 ± 1.91 , $p=0.007$). Stress symptom scores were also significantly higher in short vs. not short sleepers (ASDS scores: 25.68 ± 11.15 vs. 22.57 ± 8.89 , $p<0.001$) at baseline. A higher proportion of participants reporting short vs. not short sleep indicated use of medication for sleep (25.3% vs. 13.1%, $p<0.001$). A total of 142 participants experienced an ED or hospital readmission within 180 days following ACS evaluation. A greater proportion of participants with short sleep vs. not short sleep experienced an ED/hospital readmission (33.0% vs. 20.4%; $p=0.001$) (Table 1).

Short sleep duration was associated with increased risk of ED/hospital readmission within 6 months following ACS evaluation (HR = 2.03; 95% CI: 1.12 – 3.66) in the model adjusted for age, sex, race/ethnicity, clinical severity, cardiac and renal markers, depression, ASD, and including a sleep duration $\times$ ACS status interaction (Table 2, Figure 1). The short sleep duration (yes/no) $\times$ verified ACS (yes/no) interaction term was not significant (Table 2). A total of 34 participants (5.9% of full sample) indicated sleep duration >8 hours per night (i.e. long duration sleep). Since long sleep duration has been associated with adverse health outcomes, we re-analyzed the data after removing these participants from the normative sleep group. In these exploratory analyses, short sleep duration remained associated with

increased risk of ED/hospital readmission in the adjusted model (HR = 2.09; 95% CI: 1.13 – 3.88).

Discussion

We report that short sleep duration in the month following hospital evaluation for ACS is prevalent, present in more than 1 in 3 such patients. Individuals reporting short sleep duration, compared to those who reported sleep longer than 6 hours per night, were more likely to be female, black, use medications to aid sleep, and score higher for depression and acute stress. Our main finding was that short sleep duration was associated with over two times the risk of 6-month all-cause ED/hospital readmission following ACS evaluation. These results suggest that sleep duration following ACS is an important health behavior to consider for optimizing outcomes following an evaluation for ACS.

Although not studied here, short sleep duration may confer cardiovascular health risk through several physiologic pathways, such as increased blood pressure, inflammation, insulin resistance, sympathetic activation, endothelial dysfunction (2). Inflammation may not only be a response of short sleep duration, but systemic inflammation following ACS may also contribute to sleep disturbances, as well as worsened mood and fatigue (32). Another possibility is that short sleep duration may increase risk by impacting adherence to various health behaviors, including physical activity. Short-sleeping individuals have lower levels of physical activity compared to those with normal sleep duration (33). Individuals with short sleep duration and >3 hours per day of television viewing (a surrogate marker of sedentary behavior) have an 18% increased risk of CVD mortality relative to those with normal sleep duration and ≤3 hours per day of television viewing (34). Unfortunately, we cannot determine the pathophysiologic and/or behavioral pathways by which short sleep duration may contribute to readmission risk based on current data. The role of post-hospitalization changes to physiology and behavior, and their relation to short sleep duration, in influencing long-term outcomes should be investigated. This is particularly relevant for determine the causative factors related to readmission in participants who ruled in vs. ruled out for ACS, since these bio-behavioral factors are likely to be differentially affected after discharge in cardiac and non-cardiac etiologies.

Depression is an important psychological factor to consider in the relationship between sleep and health outcomes. Sleep disruption is one of the key symptoms of depression (35), and short sleep duration (<6 hours per night) was associated with depressive symptoms both cross-sectionally and prospectively across a ~5 year follow-up (36). Depression is also prevalent in individuals with CVD, and like short sleep duration, it can contribute to worsened cardiovascular outcomes (37) and increased risk of mortality in patients with coronary heart disease (38). Higher depression (based on PHQ scores) were seen in short sleepers compared to non-short sleepers in the current cohort. The relationship between short sleep duration and ED/hospital readmission was significant after adjusting for depression.

We have also previously observed that psychological stress following ACS evaluation is associated with increased early readmission risk. In the PULSE study, high stress during and

after ACS hospitalization was associated with a tripling in risk for early (30-day) all-cause rehospitalization (39). Within the REACH cohort, high acute stress at discharge from the ACS evaluation was associated with 30-day ED/hospital readmission (13). Whereas these prior analyses considered a role of stress in early readmission within 30 days of hospital ACS evaluation, the current analyses aimed to determine how sleep duration within the 30 days following discharge is related to readmission over the subsequent 5 months. Higher stress scores were seen in short sleepers compared to non-short sleepers in the current analyses, and, similar to depression, the relationship between short sleep duration and ED/hospital readmission remained statistically significant after adjusting for ASD symptom score. These suggest that sleep is likely related to readmission independent of stress and depression. Current findings show that sleep may be an additional important psychophysiologic factor related to readmission following hospital evaluation for ACS. However, the analyses presented here do not establish sleep as a causative agent for readmission risk.

Overall, the current readmission rate was ~25% following ACS evaluation. This differs somewhat from the 60% one-year readmission rate within 1 year reported by others (1). This difference may be due to the exclusion of readmissions occurring within the first month for current analyses, not following participants until 1 year, that the sample contained a mixed group of patients with verified ACS and ultimately without ACS, and that the urban inner city setting of the hospital might not be generalizable to other environments. It is also interesting that rate of readmission differed as a function of sleep duration, whereas time to readmission did not. This may underscore the role of non-physiologic factors, such as anxiety or stress, as a contributor to ED visit or hospital readmission.

In addition to short sleep duration, an association between long sleep duration and CVD has been reported (2). Results from a meta-analysis have shown increased risk of developing or dying from coronary heart disease, stroke, and total CVD in long vs. normative duration sleepers (28). Long sleep duration compared to normative sleep duration, was also associated with an increased risk of cardiovascular-related and all-cause death following an ACS event (4). In our cohort, only 34 patients reported sleep >8 hours per night, making it difficult to conduct a meaningful investigation of the potential “U-shaped” risk conferred by both short and long duration sleep on health outcomes. Nevertheless, the presence of long sleepers in the normative sleep duration group could potentially confound results. Overall findings on the relationship between short sleep duration and risk of readmission were unchanged when we re-ran analyses after removing those reporting sleep >8 hours. Future work should examine whether a relationship exists between long sleep duration and post-ACS hospital readmission.

A limitation of the current work is that only select PSQI sub-scale questions, on sleep duration and sleep medication use, and not the full PSQI scale, were administered to participants. As described, this analysis comes from a larger cohort study with many questionnaires examining environmental, psychosocial, and behavioral factors. In lieu of using the global PSQI score as our primary predictor of ED/hospital readmission, we focused on sleep duration. It is important to determine how overall sleep quality ratings relate to readmission, since self-reported sleep quality is related to prognosis in patients with

heart failure (40). Specifically, patients with heart failure and poor quality (PSQI global score >5) were 2.5 times more likely to experience a shorter length of cardiac event-free survival compared to patients with good sleep quality (40). We were unable to assess sleep duration in the month preceding ACS evaluation. This information would be valuable to determine whether short sleep duration emerging after the ACS evaluation is particularly related to risk for hospital readmission. Our current reliance on self-report measures of sleep is another limitation overall, and future work should utilize objective methods (e.g. wrist accelerometry or polysomnographic sleep recording) to monitor free-living sleep duration. Individuals with insomnia often experience a sleep state misperception, in which patients overestimate the degree of sleep impairment and underestimate sleep duration in comparison to objectively recorded measures (41). Therefore, objective measures of sleep in addition to other dimensions of sleep, such as sleep quality and satisfaction, should be assessed as well, since objectively defined short sleep duration combined with insomnia is associated with substantial medical morbidity and mortality (42). We did not currently assess presence, risk, or current treatment of obstructive sleep apnea in the included participants. This is important, since risk of obstructive sleep apnea was associated with increased risk of major coronary event and major adverse cardiovascular event in patients with ACS (4). It would also be important to assess the main reasons for hospital readmission, which we were unable to do here.

The current cohort includes both patients who ruled in and ruled out for ACS during their hospital evaluation for a suspected ACS event. Large numbers of patients visit the ED with ACS-like symptoms (e.g., acute chest pain, shortness of breath, left arm pain), and our current observations are consistent with others who have found that less than half are ultimately diagnosed with ACS (43). In a prior report on this REACH cohort, we observed that there were minimal differences in the somatic symptoms reported by patients with a confirmed ACS compared to those who ruled out for ACS, and that those without ACS were equally likely as those with confirmed ACS to develop elevated post-traumatic stress disorder symptoms 1-month after discharge (44). Patients with a non-cardiac etiology for ACS-like symptoms (namely, chest pain) also show a high rate of health care utilization in a 12-month period (45). This suggests that patients who rule out for ACS are still at risk for adverse long-term outcomes and increased medical costs, and as such, factors related to these outcomes should be assessed. Our current findings suggest that the relationship between short sleep duration and hospital readmission is not limited to patients who were found to have ACS at index hospitalization, thus broadening the impact and applicability of current findings. However, the potential behavioral and physiological pathways linking short sleep duration to readmission in hospitalized individuals with and without ACS should be examined in future work.

Although not tested directly here, possible implications of the current findings are that short sleep duration may represent a secondary prevention target following evaluation for ACS. Recent trials have shown that it is possible to increase sleep duration in habitual short sleepers via lifestyle interventions (46-48). Targeting and extending time in bed, combined with sleep hygiene recommendations, was found significantly increase nocturnal sleep duration and reduce blood pressure in individuals with prehypertension or hypertension (47). Cognitive behavioral therapy for insomnia (CBT-I) is also effective in improving sleep, and

potentially cardiovascular morbidity, in individuals with CVD (49). More work should be done to develop novel therapeutic options to increase sleep duration in individuals at risk for cardiac events.

Short sleep duration following ACS hospital evaluation is prevalent, and is found to be associated with increased risk of all-cause ED/hospital readmission within 6 months of discharge. Increasing attention and efforts are being made by the medical community to explore the reasons for hospital readmission and to develop interventions to reduce hospital readmissions (50). Current findings suggest that short sleep duration is an important modifiable behavioral factor that should be considered when attempting to optimize outcomes such as readmissions following a hospital evaluation for ACS.

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Abbreviations:

ACS	acute coronary syndrome
ASD	acute stress disorder
ED	emergency department
GRACE	Global Registry of Acute Coronary Events
HR	hazard ratio
PHQ	Patient Health Questionnaire
PSQI	Pittsburgh Sleep Quality Index

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Figure 1:

Covariate-adjusted Cox proportional hazards survival curves for time to emergency department (ED) or hospital readmission following ACS evaluation by sleep duration. Analyses were adjusted for age, sex, race/ethnicity, Charlson comorbidity index, Global Registry of Acute Coronary Events risk score, ACS event status (yes or no ACS event), creatinine, troponin I, Patient Health Questionnaire (PHQ)-2 score, and Acute Stress Disorder symptom scale score, and included a sleep duration x ACS status interaction term. Participants with ED/hospital readmission occurring prior to the 1-month post-ACS sleep assessment were excluded from current analyses.

Table 1:

Participant characteristics for the full sample and by sleep duration status.

	Full sample (n=576)	Sleep < 6 h (n=194)	Sleep ≥ 6 h (n=382)	P-value ^a
Age, years	61.47 (12.98)	60.92 (12.52)	61.75 (13.22)	0.46
Female, n (%)	282 (49.0%)	111 (57.2%)	171 (44.8%)	0.005
<i>Race/ethnicity</i>				
White, n (%)	103 (17.9%)	26 (13.4%)	77 (20.2%)	0.046
Black, n (%)	115 (20.0%)	48 (24.7%)	67 (17.5%)	0.041
Hispanic, n (%)	321 (55.7%)	104 (53.6%)	217 (56.8%)	0.47
Other, n (%)	37 (6.4%)	16 (8.3%)	21 (5.5%)	0.20
<i>Clinical severity</i>				
Charlson comorbidity index	1.63 (1.82)	1.77 (1.86)	1.56 (1.79)	0.18
GRACE-Risk score	92.46 (29.49)	92.50 (28.96)	92.44 (29.79)	0.98
<i>Psychological factors</i>				
PHQ-2 score	1.53 (1.97)	1.85 (2.04)	1.37 (1.91)	0.007
ASD symptom score	23.62 (9.81)	25.68 (11.15)	22.57 (8.89)	<0.001
<i>Outcomes</i>				
Sleep duration ^b , hours	6.15 (1.69)	4.27 (0.91)	7.11 (1.08)	<0.001
Use of medication for sleep ^c , n (%)	99 (17.2%)	49 (25.3%)	50 (13.1%)	<0.001
ED/hospital readmission, n (%)	142 (24.7%)	64 (33.0%)	78 (20.4%)	0.001
Time to readmission ^d , days	104.39 (42.29)	99.67 (41.71)	108.27 (42.63)	0.23

ASD: acute stress disorder; ED: emergency department; GRACE: Global Registry of Coronary Events. PHQ: Patient Health Questionnaire. Data are expressed as mean (SD) or n (%) and are compared between sleep duration groups via unpaired samples t-tests and chi-squared tests, respectively. Bold = P < 0.05.

^aP-value is for the comparison of short (< 6 h) and not short (≥ 6 h) sleep duration groups.

^bSleep duration was assessed with the question “On average, how many hours of sleep do you get per night?” at 1-month post-ACS evaluation.

^cUse of medication for sleep was assessed with the question “During the past month, how often have you taken medicine (prescribed or “over the counter”) to help you sleep?” at 1-month post-ACS evaluation. The number of participants indicating use at least once per week is indicated.

^dTime to readmission calculated only for those with an ED/hospital readmission event within 180 days of initial ACS evaluation discharge, while excluding those with an event before 30-day sleep assessment.

Table 2:

Covariate-adjusted Cox proportional hazard model results for time to emergency department (ED) or hospital readmission following ACS evaluation.

	Regression coefficient	Standard error	P-value	Hazard ratio	95% CI
Age	−0.031	0.013	0.014	0.970	0.946–0.994
Sex (0=Female, 1=Male)	−0.013	0.180	0.94	0.987	0.639–1.405
Race/Ethnicity, White (0=White, 1=Hispanic)	−0.087	0.251	0.73	0.917	0.560–1.500
Race/Ethnicity, Black (0=Black, 1=Hispanic)	−0.111	0.225	0.62	0.895	0.576–1.392
Race/Ethnicity, Other (0=Other, 1=Hispanic)	0.483	0.317	0.13	1.621	0.871–3.018
Charlson comorbidity index	0.088	0.056	0.12	1.092	0.978–1.218
GRACE-Risk score	0.017	0.006	0.003	1.018	1.006–1.029
Troponin I	−0.717	0.600	0.23	0.488	0.150–1.583
Creatinine	0.146	0.061	0.017	1.157	1.027–1.303
PHQ-2 score	−0.027	0.047	0.56	0.973	0.887–1.067
ASD symptom score	0.007	0.009	0.49	1.007	0.988–1.025
Sleep duration (0=Short, 1=Not short)	0.706	0.302	0.019	2.026	1.121–3.662
ACS status (0=No ACS, 1=Yes ACS)	0.185	0.251	0.46	1.203	0.735–1.967
Sleep category × ACS status	−0.376	0.364	0.30	0.687	0.336–1.403

For categorical variables, second variable (1) is reference. ACS: acute coronary syndrome; ASD: acute stress disorder; CI: Confidence interval; GRACE: Global Registry of Coronary Events; HR: Hazard ratio; PHQ: Patient Health Questionnaire.