Sleep Duration and Mortality in Patients With Coronary Artery Disease

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Extremes in sleep duration are associated with higher cardiovascular risk in the general population, but their impact in patients with documented coronary artery disease (CAD) remains unknown and potentially of clinical significance. We hypothesized that both short and long sleep duration are associated with higher mortality in CAD. We inquired about sleep durations in 2,846 patients enrolled in the Emory Cardiovascular Biobank (mean age 64 years, 38% female, 23% Black, and 82% with obstructive CAD, defined by positive coronary angiography), who were then followed for all-cause and cardiovascular mortality. Multivariate Cox proportional hazard models were calculated to examine the association of sleep duration and mortality. Sleep durations of <6.5 hours (short), ≥6.5 to <7.5 hours (normal), and ≥7.5 hours (long) were reported by 39%, 26% and 35% of the cohort, respectively. On follow-up (median 2.8 years), mortality rates were 15%, 11%, and 17%, respectively. After adjusting for demographics and risk factors, both short and long sleep duration were associated with higher all-cause mortality (hazard ratio 1.44, 95% confidence interval [1.10 to 1.89], and 1.41 [1.08 to 1.85], respectively). A similar pattern was demonstrated for cardiovascular mortality only for short (hazard ratio 1.48 [1.05 to 2.09]), but not long sleep duration. In conclusion, in patients with frank CAD, both short and long sleep duration were independently associated with higher all-cause mortality, and short sleep was independently associated with higher cardiovascular mortality. In conclusion, our study is the first to extend the observations of sleep duration and mortality from population-based studies to patients with documented cardiac disease. © 2018 Elsevier Inc. All rights reserved. (Am J Cardiol 2019;123:874−881)

Many population-based epidemiologic studies have shown that both short and long reported sleep durations are associated with cardiovascular mortality and morbidity,[1,2] but whether the length of sleep that a patient reports has implications in a clinical setting is far from certain. Self-reports about sleep are subject to many sources of error, including but not limited to: inherent lack of correlation with objective markers,[3] imprecision based on poor recall or inadequate reporting,[4] or psychiatric disorder.[5] In the context of a patient in a lab immediately before cardiac catheterization, one could envision additional stressors that would further erode the value of this estimate. In this study, we report on our experience of routinely inquiring about sleep duration in a cardiac population in a catheterization laboratory. Specifically, we examined prospectively cardiac events and morbidities subsequent to this procedure.

Methods

A total of 2,846 patients with completed sleep questionnaires were recruited between 2004 and 2016 as part of the Emory Cardiovascular Biobank,[6] a prospective registry of consecutive patients who underwent cardiac catheterization for suspected or known coronary artery disease (CAD) across Emory Healthcare sites. Patients with congenital heart disease, severe valvular heart disease, severe anemia, recent blood transfusion, myocarditis, active inflammatory diseases, and cancer and cardiac transplant were excluded. Recruited patients were interviewed at the time of enrollment to collect demographic characteristics and medical history. Risk factors were determined by physician diagnoses or self-reported treatment for conditions such as hypertension, hyperlipidemia, diabetes mellitus, history of smoking, and history of prior myocardial infarction (MI). Hours of daily sleep were reported as part of a self-administered enrollment questionnaire. Coronary angiograms from the index cardiac catheterization at the time of enrollment were available in 89% of participants and reviewed to

calculate Gensini score,[7] a quantitative scoring system of coronary luminal narrowing. The presence of obstructive CAD, defined as ≥50% luminal narrowing in a major epicardial vessel, was also assessed in 89% of the patients. Presentation with acute MI at enrollment and coronary revascularization as a result of the index cardiac catheterization were determined. The study was approved by the Institutional Review Board of Emory University and all patients provided written informed consent.

Subjects were asked to provide a free-text response to the question: "How many hours of sleep do you usually get each night (or when you usually sleep)?" Although the majority of the subjects reported in whole numbers of hours, 9 subjects reported to the first decimal place, for example, 8.5 hours. The reported sleep duration was categorized into short (< 6.5 hours per day), normal (≥6.5 to <7.5 hours per day), or long (≥7.5 hours per day) sleep duration, for the data analysis. Because categories of normal, short and long sleep duration often vary across studies (see Discussion), we also analyzed our data using 1-hour interval bins to examine the extent to which associations might occur in a more graded manner.

Follow-up was conducted by independent personnel blinded to the angiographic, sleep, and clinical data. All-cause and cardiovascular-specific mortality was determined through verbal communications with family, Georgia vital records, and the Social Security Death Index. Medical records and death certificates were obtained and reviewed by an adjudication committee of 3 physicians also blinded to the data. Cardiovascular death was defined as death attributable to an ischemic cardiovascular cause (fatal MI, ischemic stroke, and peripheral arterial disease), vascular cause, or sudden death attributable to an unknown but presumed cardiovascular cause in high-risk patients.

Continuous variables were presented as means (standard deviation) or as median (interquartile range) and categorical variables were reported as frequency counts and proportions (%). Chi-square test was used to compare proportions, whereas one-way analysis of variance with Tukey posthoc analysis was conducted to determine whether differences in continuous variables existed between groups stratified by sleep duration. Multivariable analysis to identify variables independently associated with sleep duration was performed using multinomial logistic regression. The covariates included age, sex (male vs female), race (Black vs non-Black), body mass index (BMI), hypertension, diabetes, hyperlipidemia, smoking history, prior MI, heart failure, acute myocardial infarction at enrollment (Y or N), revascularization (Y or N) at enrollment, and obstructive CAD (Y or N; defined by the presence of ≥50% obstructive lesion in any of the major epicardial vessels on coronary angiography at enrollment).

Survival analysis comparing patients stratified according to sleep duration was performed using Kaplan-Meier survival curves, log-rank tests as well as Cox proportional hazards modeling with the aforementioned covariates for all-cause death and cardiovascular death. Sensitivity analysis was performed to determine whether the association with outcomes differed with respect to the presence of the individual covariates by including the interaction term of sleep duration × the covariate of interest. Proportional

hazards assumption was examined by plotting Schoenfeld residuals for each covariate against time as well as including an interaction term of each covariate by time in the Cox models, and no significant violations were observed. Two-tailed p values <0.05 were considered statistically significant, and all analyses were performed with SPSS 24 (IBM, Armonk, New York).

Results

Overall, the cohort comprised of 2,846 subjects with a mean age of 64 years, 38% women and 23% Black (Table 1). The mean duration of daily sleep was 6.8 ± 1.5 hours. Overall, 39% of subjects reported short (<6.5 hours per day), 35% reported long (≥7.5 hours per day), and 26% reported normal duration of sleep (≥6.5 to <7.5 hours per day; Table 1).

Subjects reporting short duration of sleep were likely to be younger, female, and Black with higher BMI, diabetes, and heart failure than those with normal sleep duration on univariate analysis (Table 1). Patients with long duration of sleep were older and more likely to have a history of hyperlipidemia, smoking, and prior MI than those with normal sleep duration (Table 1). In multinomial logistic regression analyses, independent predictors of short sleep duration were female sex, Black race, and higher BMI, whereas older age and history of smoking were independently associated with long sleep duration (Table 2). There was no significant difference in the prevalence of obstructive CAD at enrollment among the 3 groups of sleep duration, whereas there was statistically insignificant increase in Gensini score among those with long sleep compared with those with short sleep duration (p = 0.06; Table 1). However, neither obstructive CAD nor Gensini score was predictive of either short or long sleep duration (Table 2).

During a median 2.8-year follow-up period, there were 412 (15%) all-cause deaths and 251(9%) cardiovascular deaths (Table 1). Kaplan-Meier survival analysis revealed that all-cause mortality was significantly different among the groups reporting short (15%), normal (11%), and long (17%) sleep duration (Log-rank p = 0.003, Figure 1). Unadjusted Cox proportional hazard model showed that compared with normal sleep duration, both short and long sleep duration were associated with higher all-cause mortality rate (Table 3, Model 1), which remained significant after adjusting for age, sex, race, BMI, hypertension, diabetes, hyperlipidemia, history of smoking, history of prior MI, and heart failure (hazard ratio [HR] 1.44, 95% confidence interval [1.10 to 1.89], and 1.41 [1.08 to 1.85], respectively; Table 3, Model 2) and after adjustment for CAD severity (Table 3, Model 3). We also calculated the risk of all-cause mortality sequentially with a 1-hour incremental change from the reference duration of sleep (≥6.5 to <7.5 hours per day) in the fully adjusted model (Model 3). The adjusted risk of all-cause mortality increased with increasing and decreasing duration of sleep compared with those reporting the reference duration of daily sleep. Specifically, those with extremely short sleep duration (<4.5 hours per day) had an adjusted HR of 1.96 and those with extremely long ≥8.5 hours of sleep per day had a HR 1.84 for all-

Table 1
Baseline characteristics and incident clinical outcomes according to the duration of daily sleep*

Variable	All (n = 2,846)	Short (< 6.5 h) (n = 1,119)	Normal (≥6.5 to <7.5 h) (n = 741)	Long (≥ 7.5 h) (n = 986)	Overall p value	p Value for pairwise comparison		
						Normal versus short	Normal versus long	Short versus long
Age (years)	64 ± 13	62 ± 12	64 ± 12	66 ± 13	**<0.001**	**0.006**	**<0.001**	**<0.001**
Women	1071 (38%)	472 (42%)	254 (34%)	345 (35%)	**<0.001**	**0.001**	0.76	**0.001**
Black	642 (23%)	372 (33%)	124 (17%)	146 (15%)	**<0.001**	**<0.001**	0.28	**<0.001**
Body mass index (kg/m^2)	30 ± 6	31 ± 7	30 ± 6	29 ± 6	**<0.001**	**<0.001**	0.61	**<0.001**
Hypertension	2427 (85%)	968 (87%)	624 (84%)	836 (85%)	0.37	0.20	0.80	0.27
Diabetes mellitus	1064 (38%)	441 (40%)	258 (35%)	365 (37%)	0.13	**0.05**	0.34	0.27
Hyperlipidemia[†]	2139 (75%)	838 (75%)	535 (72%)	766 (78%)	**0.04**	0.17	**0.01**	0.17
Smoker	2067 (73%)	800 (72%)	522 (70%)	745 (76%)	**0.03**	0.63	**0.02**	**0.04**
Prior MI	642 (23%)	241 (22%)	149 (21%)	252 (26%)	**0.02**	0.46	**0.01**	**0.04**
Heart failure	987 (35%)	412 (37%)	230 (31%)	345 (35%)	**0.04**	**0.01**	0.09	0.38
Ejection fraction (%)	53 ± 12	53 ± 13	54 ± 11	52 ± 13	**0.01**	**0.04**	**0.02**	0.88
Gensini score, points	86 [2,240]	80 [0,234]	85 [2,244]	112 [4,256]	0.07	0.91	0.83	0.06
Obstructive CAD[‡]	2082 (82%)	792 (81%)	542 (81%)	748 (84%)	0.20	0.68	0.24	0.08
Acute MI at enrollment	228 (8%)	90 (8%)	60 (8%)	78 (8%)	0.99	0.97	0.89	0.97
Revascularization at enrollment	941 (33%)	373 (33%)	253 (34%)	315 (32%)	0.61	0.72	0.34	0.50
All-cause death	412 (15%)	166 (15%)	81 (11%)	165 (17%)	**0.003**	**0.02**	**0.001**	**0.05**
Cardiovascular death	251 (9%)	111 (10%)	50 (7%)	90 (9%)	0.06	**0.02**	0.07	0.77
Myocardial infarction	107 (4%)	42 (4%)	22 (3%)	43 (4%)	0.32	0.36	0.13	0.99
Coronary revascularization	587 (21%)	236 (21%)	150 (20%)	201 (20%)	0.88	0.66	0.94	0.73
Stroke	68 (2%)	25 (2%)	18 (2%)	25 (3%)	0.90	0.78	0.89	0.65

Boldface indicates statistically significant values.

Abbreviations: CAD = coronary artery disease; MI = myocardial infraction.

* Values are mean (SD), median [25th and 75th interquartile range], or n (%).

[†] Defined by physician diagnosis in medical charts.

[‡] Obstructive coronary artery disease (CAD) is defined by the presence of ≥50% obstructive lesion in any of the major epicardial vessels on coronary angiography at enrollment.

cause mortality compared with those with a normal sleep duration (Figure 2).

Cardiovascular mortality rates were also significantly different among the 3 groups of short (10%), normal (7%), and long (9%) sleep duration in the Kaplan-Meier survival analysis (Log-rank p = 0.035, Figure 1). Univariate Cox regression model demonstrated that compared with normal sleep, short sleep duration was associated with higher risk of cardiovascular mortality (Table 3, Model 1), which remained significant after multivariate adjustment for the

Table 2
Multinomial logistic regression of daily sleep duration and baseline demographic and clinical characteristics

Variable	Short (<6.5 h) versus Normal (≥6.5 to <7.5 h)		Long (≥8.5 h) versus Normal (≥6.5 to <7.5 h)	
	OR, 95% CI	p Value	OR, 95% C.I.	p Value
Age, per increase of 10 years	0.94 (0.85 - 1.03)	0.17	1.13 (1.03 - 1.25)	**0.014**
Body mass index, per 5kg/m^2	1.11 (1.01 - 1.21)	**0.027**	0.99 (0.90 - 1.08)	0.75
Women	1.34 (1.07 - 1.68)	**0.011**	1.01 (0.80 - 1.27)	0.96
Black	1.95 (1.49 - 2.57)	**<0.001**	0.82 (0.60 - 1.11)	0.20
Hypertension	1.00 (0.73 - 1.38)	0.99	0.88 (0.64 - 1.20)	0.88
Diabetes mellitus	1.00 (0.80 - 1.27)	0.98	1.08 (0.85 - 1.36)	0.54
Hyperlipidemia	1.28 (0.99 - 1.66)	0.06	1.27 (0.98 - 1.65)	0.07
Smoker	1.11 (0.88 - 1.40)	0.40	1.36 (1.07 - 1.73)	**0.013**
Prior MI	1.03 (0.79 - 1.35)	0.83	1.26 (0.97 - 1.65)	0.09
Heart failure	1.10 (0.87 - 1.39)	0.42	1.12 (0.88 - 1.42)	0.35
Acute MI at enrollment	1.08 (0.72 − 1.62)	0.71	1.03 (0.69 − 1.55)	0.88
Revascularization at enrollment	1.07 (0.84 − 1.36)	0.57	0.85 (0.67 − 1.08)	0.19
Gensini score, per 10 points	1.00 (1.00 − 1.01)	0.58	1.00 (0.99 − 1.01)	0.99
Obstructive CAD*	1.04 (0.79 - 1.38)	0.77	0.98 (0.73 - 1.31)	0.88

Boldface indicates statistically significant values.

Abbreviations: CAD = coronary artery disease; CI = confidence interval; MI = myocardial infraction; OR = odds ratio.

* Obstructive coronary artery disease (CAD) is defined by the presence of ≥50% obstructive lesion in any of the major epicardial vessels on coronary angiography at enrollment.
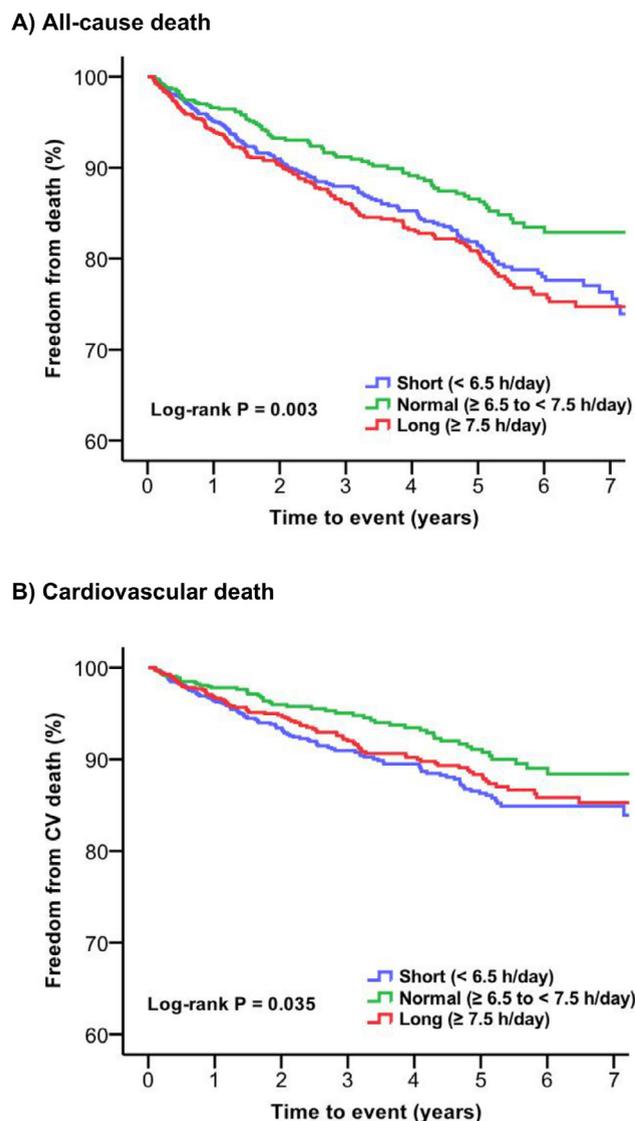
A) All-cause death

B) Cardiovascular death

Figure 1. Kaplan-Meier curves for *(A)* all-cause and *(B)* cardiovascular (CV) death stratified by the duration of daily sleep.

aforementioned covariates (HR 1.48 [1.05 to 2.09]; Table 3, Model 2) and for CAD severity (Table 3, Model 3). We also calculated cardiovascular mortality rates sequentially with a 1-hour incremental change from the reference ($\geq$6.5 hours to <7.5 hours per day) in the fully adjusted model (Model 3). Cardiovascular mortality rates increased with decreasing duration of sleep compared with those reporting the reference duration of sleep. Specifically, those with extremely short sleep duration (<4.5 hours per day) had an adjusted HR of 2.04, but there was no significant increase in risk with increasing sleep duration (Figure 2). Treating noncardiovascular death as a competing risk did not affect the results of cardiovascular mortality and sleep duration.

There was no significant difference in the incident MI rates during follow-up (Table 1). However, those with normal sleep duration had fewer number of total MIs (pre-enrollment, at enrollment, and incident MIs combined; 26 %) than those with long sleep duration (30%; p = 0.035) whereas the difference with those with short sleep duration (28%) was statistically insignificant (p = 0.28). In addition, there were no significant differences in incident coronary revascularization or stroke events among the 3 groups of sleep duration (Table 1).

In sensitivity analysis, the effect of long sleep duration for all-cause mortality differed significantly by BMI (p value for interaction = 0.02) and the presence of acute MI at enrollment (p value for interaction = 0.03) with higher mortality only in those with BMI $\leq$30 kg/m^2 and without a history of MI (Figure 3; Table 1S). There were no significant interactions with the other examined demographic or clinical variables for the association between short sleep duration and all-cause mortality. Similarly, the association between long sleep duration and cardiovascular mortality differed by BMI (p value for interaction = 0.02) where long duration of sleep was associated with higher cardiovascular mortality among those with BMI $\leq$30kg/m^2, not in those with BMI >30kg/m^2 (Figure 4; Table 2S). Otherwise, there was no other significant interaction with the examined demographic or clinical variables for the relation between sleep duration and cardiovascular mortality.

Finally, although we were underpowered to examine associations between sleep durations and all-cause and

Table 3
Association between the duration of daily sleep and all-cause / cardiovascular mortality

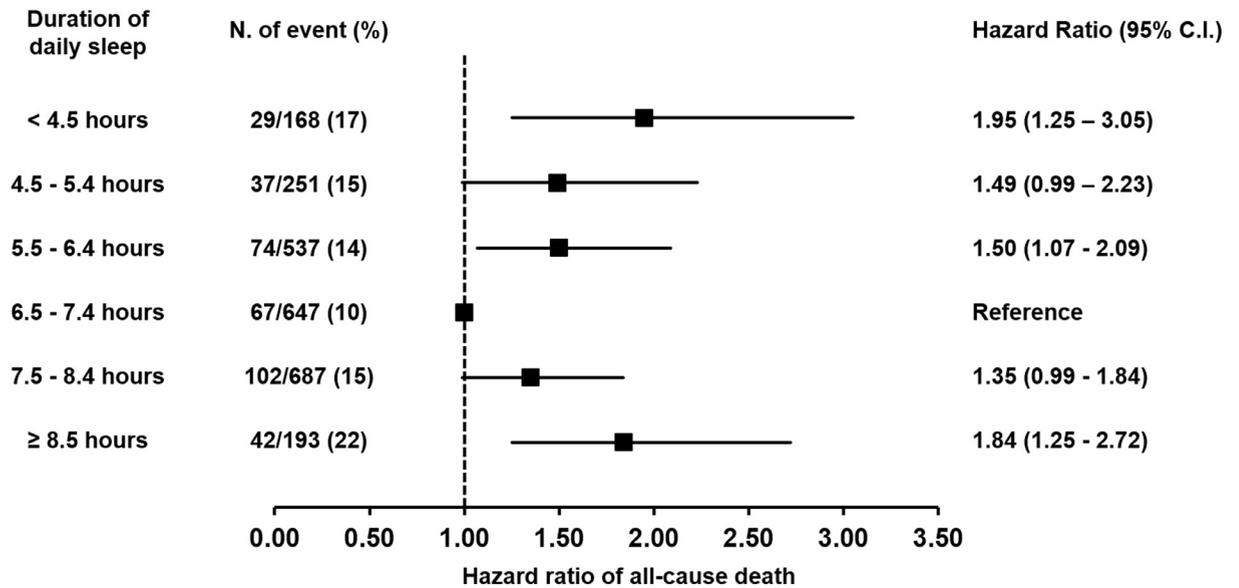| Outcome	Model	Short versus normal		Long versus normal	
		HR, 95% CI	p Value	HR, 95% CI	p Value
All death	Model 1 (Unadjusted)	1.43 (1.09-1.86)	**0.009**	1.58 (1.21-2.06)	**0.001**
	Model 2 (Model 1 + CV risk factors*)	1.44 (1.10-1.89)	**0.009**	1.41 (1.08-1.85)	**0.013**
	Model 3 (Model 2 + CAD severity†)	1.56 (1.16-2.10)	**0.003**	1.47 (1.10-1.96)	**0.010**
Cardiovascular death	Model 1 (Unadjusted)	1.55 (1.11-2.16)	**0.011**	1.40 (0.99-1.98)	0.056
	Model 2 (Model 1 + CV risk factors*)	1.48 (1.05-2.09)	**0.026**	1.24 (0.87-1.77)	0.229
	Model 3 (Model 2 + CAD severity†)	1.49 (1.03-2.15)	**0.035**	1.19 (0.82-1.73)	0.371

Boldface indicates statistically significant values.

Abbreviations: CAD = coronary artery disease; CI = confidence interval; CV = cardiovascular; HR = hazard ratio.

* Includes age (continuous), sex (male vs female), race (Black vs non-Black), body mass index (continuous), hypertension (Y or N), diabetes mellitus (Y or N), hyperlipidemia (Y or N), history of smoking (Y or N), prior MI (Y or N), and heart failure (Y or N)

† Includes acute myocardial infarction at enrollment (Y or N), revascularization at enrollment (Y or N), and obstructive CAD (Y or N; defined by the presence of $\geq$50% obstructive lesion in any of the major epicardial vessels on coronary angiography at enrollment).

A) All-cause death

Duration of daily sleep	N. of event (%)		Hazard Ratio (95% C.I.)
< 4.5 hours	29/168 (17)		1.95 (1.25 – 3.05)
4.5 - 5.4 hours	37/251 (15)		1.49 (0.99 – 2.23)
5.5 - 6.4 hours	74/537 (14)		1.50 (1.07 - 2.09)
6.5 - 7.4 hours	67/647 (10)		Reference
7.5 - 8.4 hours	102/687 (15)		1.35 (0.99 - 1.84)
≥ 8.5 hours	42/193 (22)		1.84 (1.25 - 2.72)

Hazard ratio of all-cause death

B) Cardiovascular death

Duration of daily sleep	N. of event (%)		Hazard Ratio (95% C.I.)
< 4.5 hours	21/168 (13)		2.04 (1.19 - 3.49)
4.5 - 5.4 hours	18/251 (7)		1.08 (0.62 - 1.87)
5.5 - 6.4 hours	50/537 (9)		1.53 (1.02 - 2.31)
6.5 - 7.4 hours	43/647 (7)		Reference
7.5 - 8.4 hours	59/687 (9)		1.21 (0.81 - 1.79)
≥ 8.5 hours	17/193 (9)		1.13 (0.64 - 1.99)

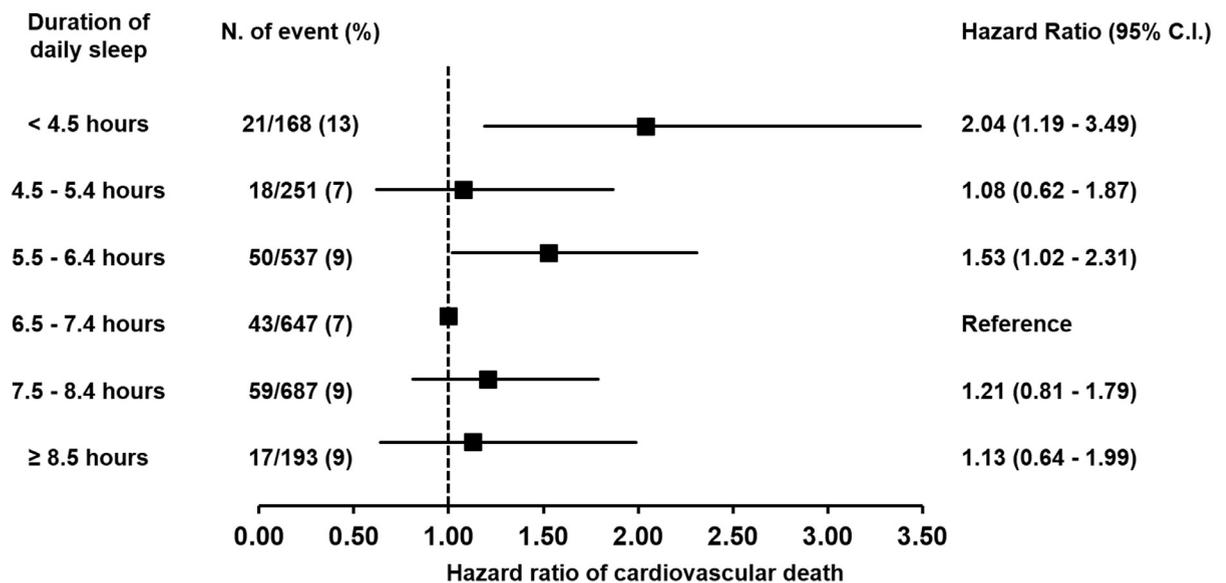Hazard ratio of cardiovascular death

Figure 2. Adjusted hazard ratio of all-cause *(A)* and cardiovascular *(B)* mortality stratified by the hours of daily sleep duration. The model is adjusted for age, sex, race, body mass index, hypertension, diabetes, hyperlipidemia, smoking history, prior myocardial infarction, heart failure, acute myocardial infarction at enrollment, revascularization at enrollment, and obstructive coronary artery disease. CI = confidence interval; N = number.

cardiovascular mortality in individuals without definitive evidence of CAD, we also tested for interaction between individuals with a Gensini score >0 when compared with all other individuals and found no evidence of interaction (p values for both short vs normal and long vs normal, as well as for both all-cause and cardiovascular mortality ranged from 0.29 to 0.67; data not shown).

Discussion

In a large population of patients with CAD, we observed that compared with those with normal sleep duration (≥6.5 to <7.5 hours), patients with either short or long sleep duration (<6.5 and ≥7.5 hours) had a higher all-cause mortality

rate. Moreover, short sleep duration was associated with a higher cardiovascular mortality rate. To our knowledge, this is the first study to investigate the adverse impact of sleep duration in a population with CAD.

Women, Black race, and higher BMI were independent predictors of short sleep duration. Racial differences in sleep duration have been reported,[8] likely mediated by genetic and socio-ecological influences.[9] Although not all studies found that shorter sleep duration occurred more commonly in women,[10,11] the association between higher BMI and shorter sleep duration is well-established, probably due to associated changes in leptin and ghrelin.[12] We also found that older individuals and smokers had longer sleep duration. Shorter sleep duration and decreased sleep
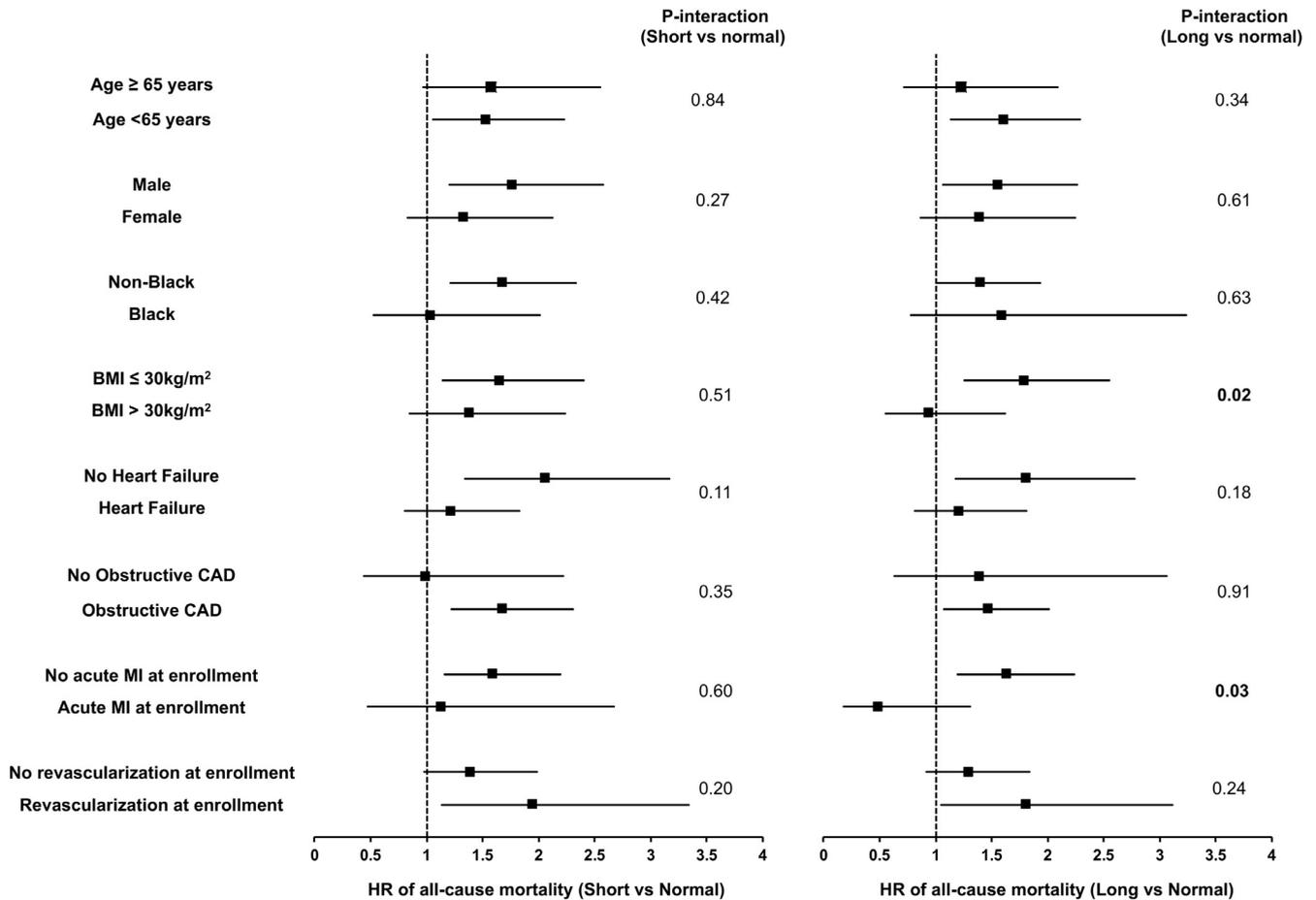
Figure 3. Sensitivity analysis of the association between all-cause mortality and daily sleep duration. All models are adjusted for age, sex, race, body mass index, hypertension, diabetes, hyperlipidemia, smoking history, prior myocardial infarction, heart failure, acute myocardial infarction at enrollment, revascularization at enrollment, and obstructive coronary artery disease. BMI = body mass index; CAD = coronary artery disease; MI = myocardial infarction.

quality/efficiency has been previously reported in older individuals,[13] suggesting that our findings reflect decreased sleep efficiency and longer time in bed rather than longer sleep time *per se*. In keeping with previous reports, we also found that smoking was associated with longer sleep duration.[14,15]

In comparison to normal sleep duration (≥6.5 to <7.5 hours), both short (<6.5 hours) and long (≥7.5 hours) sleep duration were associated with a higher all-cause mortality by 56% and 47%, respectively, even after adjustment for demographic and risk factor differences. Our findings confirm previous studies that reported a U-shaped association between sleep duration and higher mortality in population-based, nonclinic cohorts with relatively low prevalence of cardiac disease.[16–19] Cardiovascular mortality was also 49% higher and independently associated with short sleep duration. The 19% adjusted increase in cardiovascular mortality rate in those with long sleep duration was not statistically significant, findings similar to some[1,2] but not other population-based studies.[17] Potential reasons for this discrepancy include statistical power, and probability that the higher cardiovascular mortality with long sleep is mediated by cardiovascular risk factors and demography that was not fully adjusted for in previous studies.

As "normal" duration of daily sleep has not been clearly defined in the literature, sleep duration ranging from 6 to 9 hours have been used as a reference range previously.[1,18,19] To clarify this further, we also examined mortality risk with 1-hour increments of sleep duration from the reference group (≥6.5 to 7.5 hours) and found a higher mortality rate in those with extremes of both increasing and decreasing sleep duration, with 96% increase in those sleeping ≤4.5 hours and 84% increase in those sleeping ≥8.5 hours.

The mechanisms underlying the association between sleep duration and mortality remain unknown.[20,21] Short sleep duration has been associated with cardiometabolic syndrome[22] and subclinical cardiovascular disease denoted by coronary calcification,[23] carotid intimal thickening,[24] and endothelial dysfunction.[25] Potential mechanisms for long sleep duration include sleep fragmentation, fatigue, lack of physiological challenge, depression, low socioeconomic status, obstructive sleep apnea, cancer, and respiratory disase.[18,21,26,27] Finally, higher cardiovascular mortality with long sleep duration may be mediated through other cardiovascular risk factors, as adjustment for these attenuated the association between long sleep duration and cardiovascular mortality in our cohort.
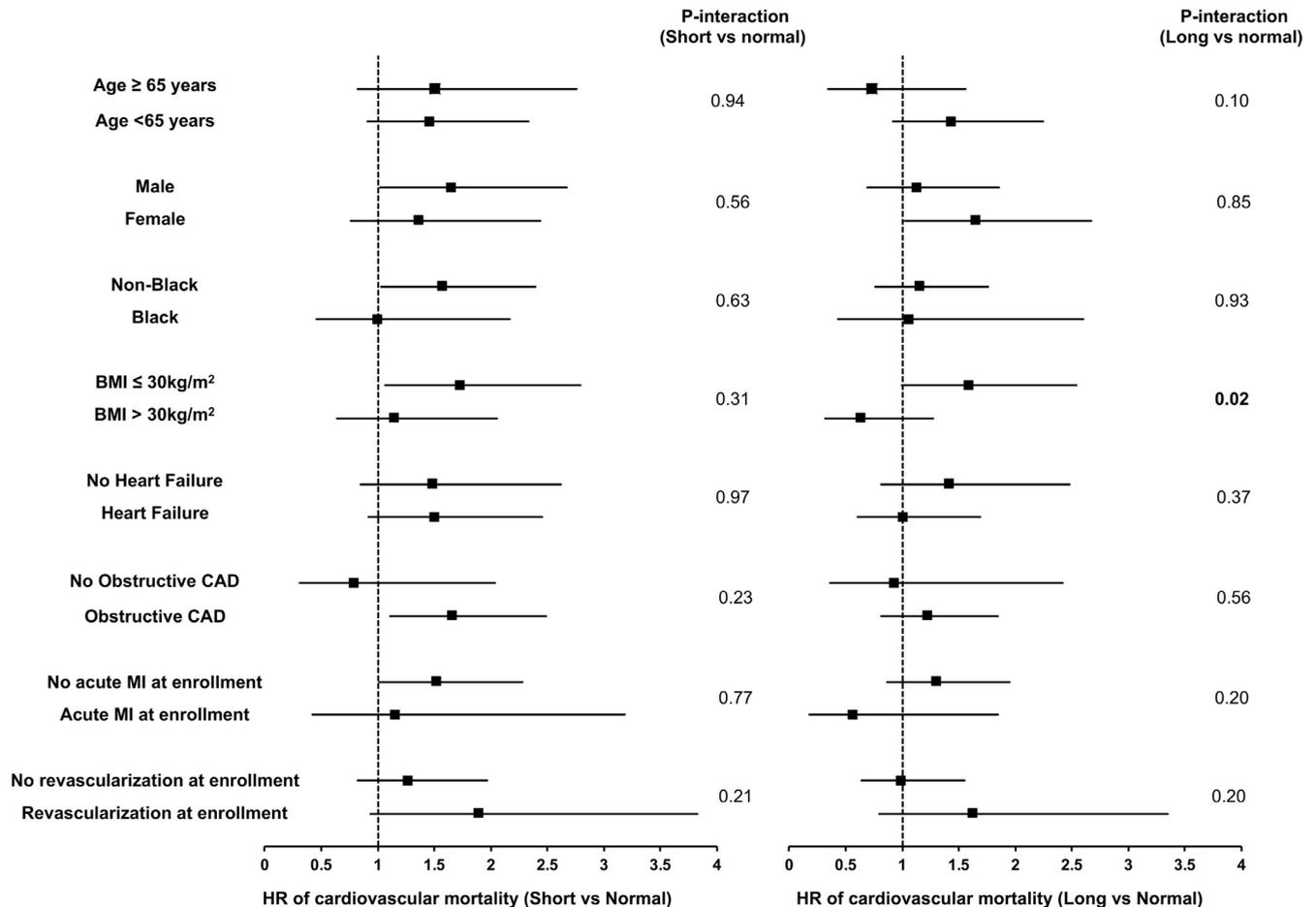
Figure 4. Sensitivity analysis of the association between cardiovascular mortality and daily sleep duration. All models are adjusted for age, sex, race, body mass index, hypertension, diabetes, hyperlipidemia, smoking history, prior myocardial infarction, heart failure, acute myocardial infarction at enrollment, revascularization at enrollment, and obstructive coronary artery disease. BMI = body mass index; CAD = coronary artery disease; MI = myocardial infarction.

The association between mortality and sleep duration was relatively similar across different subgroups stratified by demographic and clinical characteristics. However, higher mortality with longer sleep duration was found in nonobese subjects, but not in obese subjects. A strong correlation has been reported between obesity, short sleep duration, and poor sleep quality, whereas the evidence is not robust for long sleep duration.[28] Thus, it is possible that the report of long sleep duration from an obese person may be indicative of relatively better sleep quality and structure, nullifying the true adverse impact of long sleep duration. Second, higher risk of all-cause mortality with long sleep duration was only seen in patients without acute MI at enrollment, but not in those with acute MI, a difference that is most likely driven by the large number of subjects without acute MI (92%) in our cohort.

Several limitations of our analysis should be noted. Single-center enrollment from patients who underwent cardiac catheterization limits the generalizability. Second, as in previous epidemiologic cohorts, sleep duration was self-reported. However, studies utilizing wrist actigraphy have confirmed close correlation between self-reported and objective measurements, although there are also discrepancies in some subgroups.[29] Third, self-reported sleep

duration may represent a proxy for other aspects of sleep such as time in bed and sleep quality, which could be vulnerable to biases of reporting individuals. Furthermore, sleep duration was assessed once at the baseline, but there is evidence showing the change in sleep duration having prognostic implications.[30] Finally, we did not assess sleep-related breathing disorders, which may impact the duration of sleep reported by this otherwise infirm population.

In conclusion, we demonstrated in a cohort of patients with CAD that both short (<6.5 hours per day) and long ($\geq$ 7.5 hour per day) sleep duration compared with normal sleep duration ($\geq$6.5 to <7.5 hours) were independently associated with higher all-cause mortality, and mortality from cardiovascular causes was higher in those with short sleep duration. These results extend the findings from the population-based cohorts to those with documented CAD.

Disclosures

Dr. Bliwise serves as a consultant for Merck, Jazz, Ferring, Eisai, and Respicardia, and as a speaker for Merck. None of the other authors report conflict of interest relevant to this article.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.1016/j.amjcard.2018.11.057.

1. Cappuccio FP, Cooper D, D'Elia L, Strazzullo P, Miller MA. Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. *Eur Heart J* 2011;32:1484–1492.
2. Sabanayagam C, Shankar A. Sleep duration and cardiovascular disease: results from the National Health Interview Survey. *Sleep* 2010;33:1037–1042.
3. Lauderdale DS, Knutson KL, Yan LL, Liu K, Rathouz PJ. Self-reported and measured sleep duration: how similar are they. *Epidemiology* 2008;19:838–845.
4. Gehrman P, Matt GE, Turingan M, Dinh Q, Ancoli-Israel S. Towards an understanding of self-reports of sleep. *J Sleep Res* 2002;11:229–236.
5. Park S, Cho MJ, Chang SM, Bae JN, Jeon HJ, Cho S-J, Kim B-S, Chung I-W, Ahn JH, Lee HW, Hong JP. Relationships of sleep duration with sociodemographic and health-related factors, psychiatric disorders and sleep disturbances in a community sample of Korean adults. *J Sleep Res* 2010;19:567–577.
6. Ko Y-A, Hayek S, Sandesara P, Samman Tahhan A, Quyyumi A. Cohort profile: the Emory Cardiovascular Biobank (EmCAB). *BMJ Open* 2017;7. e018753-e018753.
7. Gensini GG. *Coronary Arteriography*. New York, NY: Futura Pub. Co.; 1975.
8. Whinnery J, Jackson N, Rattanaumpawan P, Grandner MA. Short and long sleep duration associated with race/ethnicity, sociodemographics, and socioeconomic position. *Sleep* 2014;37:601–611.
9. Adenekan B, Pandey A, McKenzie S, Zizi F, Casimir GJ, Jean-Louis G. Sleep in America: role of racial/ethnic differences. *Sleep Med Rev* 2013;17:255–262.
10. van den Berg JF, Miedema HME, Tulen JHM, Hofman A, Neven AK, Tiemeier H. Sex differences in subjective and actigraphic sleep measures: a population-based study of elderly persons. *Sleep* 2009;32:1367–1375.
11. Polo-Kantola P, Laine A, Kronholm E, Saarinen MM, Rautava P, Aromaa M, Sillanpaa M. Gender differences in actual and preferred nocturnal sleep duration among Finnish employed population. *Maturitas* 2016;94:77–83.
12. Taheri S, Lin L, Austin D, Young T, Mignot E. Short sleep duration is associated with reduced leptin, elevated ghrelin, and increased body mass index. *PLoS Med* 2004;1:e62.
13. Ohayon MM, Carskadon MA, Guilleminault C, Vitiello MV. Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. *Sleep* 2004;27:1255–1273.
14. Tsou M-T. Association between sleep duration and health outcome in elderly Taiwanese. *Int J Gerontol* 2011;5:200–205.
15. Schoenborn CA, Adams PF. *Sleep Duration as a Correlate of Smoking, Alcohol Use, Leisure-Time Physical Inactivity, and Obesity Among Adults: United States, 2004-2006 National Health Statistics Reports*. Hyattsville, MD: National Center for Health Statistics; 2008.
16. Kripke DF, Garfinkel L, Wingard DL, Klauber MR, Marler MR. Mortality associated with sleep duration and insomnia. *Arch Gen Psychiatry* 2002;59:131–136.
17. Xiao Q, Keadle SK, Hollenbeck AR, Matthews CE. Sleep duration and total and cause-specific mortality in a large US cohort: interrelationships with physical activity, sedentary behavior, and body mass index. *Am J Epidemiol* 2014;180:997–1006.
18. Gallicchio L, Kalesan B. Sleep duration and mortality: a systematic review and meta-analysis. *J Sleep Res* 2009;18:148–158.
19. Cappuccio FP, D'Elia L, Strazzullo P, Miller MA. Sleep duration and all-cause mortality: a systematic review and meta-analysis of prospective studies. *Sleep* 2010;33:585–592.
20. Grandner MA, Hale L, Moore M, Patel NP. Mortality associated with short sleep duration: the evidence, the possible mechanisms, and the future. *Sleep Med Rev* 2010;14:191–203.
21. Grandner MA, Drummond SP. Who are the long sleepers? Towards an understanding of the mortality relationship. *Sleep Med Rev* 2007;11:341–360.
22. Grandner MA, Chakravorty S, Perlis ML, Oliver L, Gurubhagavatula I. Habitual sleep duration associated with self-reported and objectively determined cardiometabolic risk factors. *Sleep Med* 2014;15:42–50.
23. King CR, Knutson KL, Rathouz PJ, Sidney S, Liu K, Lauderdale DS. Short sleep duration and incident coronary artery calcification. *JAMA* 2008;300:2859–2866.
24. Sands MR, Lauderdale DS, Liu K, Knutson KL, Matthews KA, Eaton CB, Linkletter CD, Loucks EB. Short sleep duration is associated with carotid intima-media thickness among men in the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Stroke* 2012;43:2858–2864.
25. Hall MH, Mulukutla S, Kline CE, Samuelsson LB, Taylor BJ, Thayer JF, Krafty RT, Frank E, Kupfer DJ. Objective sleep duration is prospectively associated with endothelial health. *Sleep* 2017;40:zsw003.
26. Bliwise DL, King AC, Harris RB. Habitual sleep durations and health in a 50-65 year old population. *J Clin Epidemiol* 1994;47:35–41.
27. Yeo Y, Ma SH, Park SK, Chang SH, Shin HR, Kang D, Yoo KY. A prospective cohort study on the relationship of sleep duration with all-cause and disease-specific mortality in the Korean Multi-center Cancer Cohort study. *J Prev Med Public Health* 2013;46:271–281.
28. Spiegel K, Tasali E, Leproult R, Van Cauter E. Effects of poor and short sleep on glucose metabolism and obesity risk. *Nat Rev Endocrinol* 2009;5:253.
29. Cespedes EM, Hu FB, Redline S, Rosner B, Alcantara C, Cai J, Hall MH, Loredo JS, Mossavar-Rahmani Y, Ramos AR, Reid KJ, Shah NA, Sotres-Alvarez D, Zee PC, Wang R, Patel SR. Comparison of self-reported sleep duration with actigraphy: results from the hispanic community health study/study of Latinos Sueño Ancillary Study. *Am J Epidemiol* 2016;183:561–573.
30. Ferrie JE, Shipley MJ, Cappuccio FP, Brunner E, Miller MA, Kumari M, Marmot MG. A prospective study of change in sleep duration: associations with mortality in the Whitehall II cohort. *Sleep* 2007;30:1659–1666.