

Siesta in Healthy Adults and Coronary Mortality in the General Population

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Background: Midday napping (siesta) is common in populations with low coronary mortality, but epidemiological studies have generated conflicting results. We have undertaken an analysis based on a sizable cohort with a high frequency of napping and information on potentially confounding variables including reported comorbidity, physical activity, and diet.

Methods: Among participants in a general population cohort (the Greek European Prospective Investigation into Cancer and Nutrition [EPIC] cohort), 23 681 individuals who at enrollment had no history of coronary heart disease, stroke, or cancer and had complete information on frequency and duration of midday napping, as well as on potentially confounding variables, were followed up for a mean of 6.32 years. Data were modeled through Cox regression, using time to coronary death and treating deaths from other causes as censoring events as outcomes.

Results: Among men and women, when controlling for potential confounders and using those not taking siesta as a referent category, those taking a siesta of any frequency or duration had a coronary mortality ratio (MR) of 0.66 (95% confidence interval [CI], 0.45-0.97). Specifically, those occasionally napping had a 12% lower coronary mortality (MR, 0.88; 95% CI, 0.48-1.60), whereas those systematically napping had a 37% lower coronary mortality (MR, 0.63; 95% CI, 0.42-0.93). Among men, the inverse association was stronger when the analysis was restricted to those who were currently working at enrollment, whereas among women, a similar analysis was not possible because of the small number of deaths.

Conclusion: After controlling for potential confounders, siesta in apparently healthy individuals is inversely associated with coronary mortality, and the association was particularly evident among working men.

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THE HYPOTHESIS THAT MIDDAY napping (siesta) may reduce the risk for coronary heart disease (CHD) was proposed on the basis of ecological evidence indicating that countries where the habit is common (Mediterranean and several Latin American countries) also tend to have low mortality rates of CHD.¹ Two case-control studies in Greece provided weak evidence in support of this hypothesis^{2,3} and triggered another considerably larger case-control study in Costa Rica,⁴ as well as a number of inherently superior cohort investigations of this issue.⁵⁻⁸ The large and methodologically advanced case-control study in Costa Rica, as well as all cohort investigations, did not find an inverse association between siesta or daytime sleepiness and incidence of or mortality from

cardiovascular causes or all causes; instead, they reported mostly positive associations. However, in contrast to sleepiness, which has been exploited as an indicator of sleep disturbance, none of these earlier studies met all the criteria required for the assessment of the role siesta plays in coronary mortality among healthy individuals.

Case-control studies^{1,3,4} are problematic in the investigation of the incidence of CHD because sudden coronary deaths cannot be included in the case series. Physical activity is an important confounder because it is inversely associated with coronary incidence and mortality as well as siesta. Some information was available on physical activity in some of these studies,^{4,6} but this was not always sufficiently detailed to minimize the possibility of residual confounding.⁶ Most co-

hort studies⁵⁻⁷ were based on persons who were already elderly at enrollment and thus likely to have some comorbidity, which has been shown to be positively associated with the frequency of siesta (as well as other spells of daytime sleepiness) and with overall and coronary mortality,^{6,9} thus confounding a possible siesta-coronary mortality association.

We have evaluated the association between siesta and coronary mortality in a cohort of Greek adults in which habitual physical activity has been determined in detail,¹⁰ comorbidity at enrollment has been ascertained, and risk factors for coronary mortality, including diet, have been determined. We have evaluated the association between siesta and coronary mortality separately among currently working men (younger and healthier) and among retirees and nonworking men. The latter approach was not possible for women because in Greece middle-aged women frequently opt for home caring.

METHODS

THE GREEK EPIC STUDY

The enrollment of participants in the Greek component of the European Prospective Investigation into Cancer and Nutrition (EPIC) took place between 1994 and 1999. A total of 28 571 volunteers, aged between 20 and 86 years, were recruited from all regions of Greece. The EPIC study is being conducted in 10 European countries and is coordinated by the International Agency for Research on Cancer (IARC). Details on the design and methods of the EPIC study and the Greek cohort have been previously described.^{11,12} All procedures were in line with the Helsinki declaration for human rights, all volunteers signed informed consent forms, and the study protocol was approved by ethics committees at IARC and at the University of Athens Medical School. In Greece, study participants responded to extensive interviewer-administered questionnaires addressing lifestyle habits, usual dietary intakes, and medically substantiated history of diseases.

STUDY VARIABLES

At baseline, all individuals were asked to report whether they were taking midday naps, as well as the average duration (in 5-minute increments) and the weekly frequency of these naps. We have categorized the participants into those never taking midday naps; those taking midday naps regularly, that is, at least 3 times per week, with average nap duration of at least 30 minutes (systematic napping); and those taking midday naps irregularly, that is, either once or twice per week (frequently on weekends) or those taking short midday naps with average duration of less than 30 minutes, irrespective of the weekly frequency (occasional napping).

Individuals further reported their frequency of participation in occupational and leisure time physical activities, each of which is characterized by a multiple of resting metabolic rate (MET value).¹³ The mean time per day spent on each activity, as well as sleep, was multiplied by the MET value of the activity, and all MET-hour products were summed to produce an estimate of daily physical activity, indicating the amount of energy per kilogram of body weight expended during an average day.^{10,13} Usual dietary intake over the year preceding enrollment was assessed by an extensive validated food frequency questionnaire.^{14,15} Subsequently, a score assessing adherence to a Mediterranean diet was calculated using values from 0 (mini-

mal adherence) to 9 (maximal adherence). This Mediterranean diet score has been found to be inversely associated with mortality from all causes as well as coronary mortality.¹² Anthropometric measurements were taken, and sociodemographic and lifestyle characteristics were also recorded.

PARTICIPANTS AND FOLLOW-UP

Of the 28 571 participants, 26 886 (94.1%) were followed up at various intervals until the end of December 2005. Among the 26 886 participants who have been followed-up, 1184 were excluded because of missing values in 1 or more of the variables used in the present study. Among the 25 702 study participants, there were 2021 who, at enrollment, reported previously medically diagnosed CHD (including angina), stroke, cancer, or any combination of these. These participants were excluded from the main analyses because they have increased mortality and, independently, increased frequency of siesta, so that prevalent serious disease would act as a confounding factor. Thus, the main analyses relied on 23 681 individuals.

The mean duration of follow-up was 6.32 years. Death date and cause of death for all deceased were obtained from death certificates and other official sources, and trained physicians coded the cause of death according to the *International Statistical Classification of Diseases, 10th Revision*.

STATISTICAL ANALYSIS

All analyses were performed using the Stata statistical software (Intercooled Stata 7.0 for Windows 98/95/NT; StataCorp, College Station, Tex; 2002). Survival data were modeled through proportional hazards (Cox) regression. The Cox models were used to assess the association between siesta and coronary mortality, considering death from noncoronary causes as censoring events. Analyses were performed separately for men and women as well as separately for those who were, at enrollment, working or not working. Adjustment was done for age (continuously, expressed in 5-year increments or categorically in 5-year groups, depending on the model); smoking status (never and ex-smokers and 1-10, 11-20, 21-30, 31-40, and ≥ 41 cigarettes per day, ordered); years of education, as a socioeconomic status indicator (≤ 5 , 6-11, 12, or ≥ 13 year, ordered), body mass index (calculated as weight in kilograms divided by height in meters squared; continuous or in 3 categories [< 25 , 25-30, or ≥ 30 , depending on the model]), the ratio of the waist circumference to the hip circumference (waist-hip ratio, sex-specific tertiles, ordered), level of physical activity (sex-specific quintiles of MET-hours per day, ordered) and the Mediterranean diet score (categorical or per unit, depending on the model).

RESULTS

In a preliminary analysis of all 25 702 study participants who had no missing information, but which included those who, at enrollment, reported previously medically diagnosed CHD, stroke, or cancer ($n=2021$), there was no association between siesta and overall mortality. Indeed, those who took long siestas (exceeding 2 hours) had a statistically nonsignificant excess mortality (mortality ratio [MR], 1.14; 95% confidence interval [CI], 0.95-1.38). However, those with prevalent serious disease at enrollment had substantially increased frequency of siesta, including long siesta, making it necessary to exclude them from all analyses to avoid serious confound-

Table 1. Coronary Mortality Ratios (MRs) by Important Covariates in the Greek EPIC Cohort*

Variable†	Men				Women			
	No.	Person-Years	Deaths	MR (95% CI)	No.	Person-Years	Deaths	MR (95% CI)
Age	9569	58 992	85	1.57 (1.41-1.76)	14 112	90 774	48	2.22 (1.81-2.72)
Smoking status	9569	58 992	85	1.26 (1.08-1.47)	14 112	90 774	48	1.72 (1.11-2.66)
Education	9569	58 992	85	0.81 (0.62-1.06)	14 112	90 774	48	0.69 (0.45-1.07)
Employment status								
Currently working	7301	45 111	28	1.00	5895	38 364	6	1.00
Currently not working	2268	13 881	57	2.23 (1.21-4.11)	8217	52 410	42	0.99 (0.39-2.48)
Body mass index	9569	58 992	85	0.99 (0.94-1.04)	14 112	90 774	48	1.08 (1.02-1.13)
Waist-hip ratio	9569	58 992	85	1.17 (0.89-1.54)	14 112	90 774	48	1.58 (0.98-2.54)
Physical activity	9569	58 992	85	0.87 (0.74-1.03)	14 112	90 774	48	0.75 (0.57-0.97)
Mediterranean diet score								
0-3	2854	16 883	36	1.00	4858	30 038	25	1.00
4-5	4073	25 213	34	0.71 (0.44-1.13)	6081	39 415	17	0.60 (0.32-1.11)
6-9	2642	16 895	15	0.49 (0.26-0.89)	3173	21 322	6	0.48 (0.20-1.18)
Taking midday naps‡								
No	2052	12 550	23	1.00	4844	30 868	16	1.00
Occasionally	1436	8732	8	0.57 (0.25-1.28)	1949	12 882	7	1.50 (0.61-3.65)
Systematically	6081	37 709	54	0.53 (0.32-0.86)	7319	47 024	25	0.90 (0.48-1.68)
Yes	7517	46 442	62	0.53 (0.33-0.86)	9268	59 907	32	0.98 (0.54-1.79)

Abbreviations: CI, confidence interval; EPIC, European Prospective Investigation into Cancer and Nutrition.

*There were 23 681 participants in this study, who at enrollment were free from coronary infarct, angina, stroke or cancer. All rates are age adjusted.

†Age (continuous, expressed in 5-year increments); smoking status (never and ex-smokers, 1-10, 11-20, 21-30, 31-40, and >40 cigarettes per day, ordered); education (≤5 y, 6-11 y, 12 y, and ≥13 y, ordered); body mass index (continuous); waist-hip ratio (sex-specific tertiles, ordered); physical activity (sex-specific quintiles of resting metabolic rate, hours per day, ordered); Mediterranean diet score (from 0 to 9, categorical); and taking midday naps (categorical).

‡“No,” persons never taking midday naps; “systematically,” persons who take midday naps at least 3 times per week, with an average duration of each nap of at least 30 minutes; “occasionally,” all other participants (intermediate category); and “yes,” persons taking midday naps occasionally or systematically.

ing. Among 23 681 individuals free of serious prevalent disease at enrollment, 792 deaths have occurred during follow-up, and among these deaths, 133 were due to CHD, that is, the disease that we have hypothesized could be related to regular midday napping.^{1,2}

Table 1 gives descriptive data and age-adjusted, but not mutually adjusted, coronary MRs in relation to risk factors, separately for men and women. These data are not directly interpretable because of mutual confounding among several risk factors. Nevertheless, they point to well known associations of coronary mortality with age, smoking, and central obesity (positive), as well as education, physical activity, and Mediterranean diet score (inverse). Among men there was evidence that siesta may be inversely associated with coronary mortality, whereas among women there was no clear pattern.

Table 2 gives Cox regression-derived, mutually adjusted coronary MRs by the indicated variables, among persons who, at enrollment, had no prevalent serious disease, separately for men and women. The data suggest that associations of coronary mortality with age, smoking, education, and physical activity are stronger among women than among men, although directions are similar in the 2 sexes. Associations with BMI and waist-hip ratio can only be interpreted jointly, so that introducing them in the models mainly serves to control their confounding influences on possible associations of siesta with coronary mortality. It is worth noting that even after full adjustment, men currently not working have excess coronary mortality, a finding suggesting that unascertained morbidity, which could underlie nonemployment at enrollment,

Table 2. Cox Regression-Derived Coronary Mortality Ratios by Important Covariates in the Greek EPIC Cohort*

Variable†	Men	Women
Age	1.40 (1.19-1.64)	2.10 (1.63-2.70)
Smoking status	1.24 (1.06-1.45)	1.91 (1.22-2.98)
Education	0.87 (0.66-1.15)	0.69 (0.43-1.10)
Employment status		
Currently working	1.00	1.00
Currently not working	2.10 (1.06-4.14)	0.65 (0.24-1.77)
Body mass index	0.98 (0.92-1.04)	1.06 (1.01-1.12)
Waist-hip ratio	1.23 (0.91-1.67)	1.40 (0.86-2.28)
Physical activity	0.96 (0.79-1.15)	0.77 (0.59-1.01)
Mediterranean diet score	0.90 (0.79-1.02)	0.89 (0.74-1.06)
Taking midday naps‡		
No	1.00	1.00
Occasionally	0.58 (0.26-1.31)	1.54 (0.63-3.76)
Systematically	0.50 (0.31-0.82)	0.86 (0.46-1.62)
Yes	0.51 (0.32-0.83)	0.96 (0.52-1.75)

*Data are given as mortality ratio (95% confidence interval). There were 23 681 participants in this study, who at enrollment were free from coronary infarct, angina, stroke, or cancer.

†Age (continuous, expressed in 5-year increments); smoking status (never and ex-smokers, 1-10, 11-20, 21-30, 31-40, and >40 cigarettes per day, ordered); education (≤5 y, 6-11 y, 12 y, and ≥13 y, ordered); body mass index (continuous); waist-hip ratio (sex-specific tertiles, ordered); physical activity (sex-specific quintiles of resting metabolic rate, hours per day, ordered); Mediterranean diet score (from 0 to 9, categorical); and taking midday naps (categorical).

‡“No,” persons never taking midday naps; “systematically,” persons who take midday naps at least 3 times per week, with an average duration of each nap of at least 30 minutes; “occasionally,” all other participants (intermediate category); and “yes,” persons taking midday naps occasionally or systematically.

increases the risk of coronary death. Among women, there were only 6 deaths among the currently employed, who were generally younger, reflecting society norms among older generations in the Greek population (Table 1). With respect to siesta, among men the data indicate significant inverse associations with coronary mortality with a hint of exposure response, whereas among women there was little evidence for an inverse association. Possibly because of statistical power limitations, there was no significant sex by siesta interaction with respect to coronary mortality (P value for interaction, $>.05$ in all models), formally allowing pooling. Among men and women, when controlling for sex as well as the previously indicated potential confounders and using those not taking midday naps as a referent category, those taking midday naps of any frequency or duration had a coronary MR of 0.66 (95% CI, 0.45-0.97). Specifically, in comparison with those not taking midday naps, those occasionally napping had a 12% lower rate of coronary death (coronary MR, 0.88; 95% CI, 0.48-1.60), whereas those systematically napping had a 37% lower rate of coronary death (coronary MR, 0.63; 95% CI, 0.42-0.93). Controlling for age and BMI categorically, rather than continuously, did not materially affect the results. Moreover, we found no significant interaction between BMI and siesta with respect to coronary mortality. We have probed whether BMI, notwithstanding controlling for it, might generate residual confounding of the association between siesta and coronary mortality, but we found no such evidence. In any case, BMI and siesta were minimally associated (Spearman $r < 0.04$ in absolute terms among both men and women), making it unlikely that BMI would be an important confounder.

Because, at enrollment, most men were working, whereas most women were not working, and the apparent effect of siesta was evident among men, we have examined whether siesta could tend to reduce coronary mortality mostly among working persons. We have undertaken an analysis, separating men into those currently working (mean \pm SD age, 47.5 \pm 10.1 years; 28 deaths) and those currently not working (mean \pm SD age, 66.8 \pm 7.4 years; 57 deaths). A similar analysis for women was not possible because there were only 6 deaths among the relatively young women who were working at enrollment. The results of the analyses are given in **Table 3**. There is evidence that siesta is significantly inversely associated with coronary mortality among men who were working at enrollment, whereas among men who were not working at enrollment, the association between siesta and coronary mortality is weaker and, notwithstanding larger number of outcomes, not significant. The test for interaction, however, was not statistically significant (P value for interaction, .26).

We have examined whether among working men the association of siesta with coronary mortality was more evident among the relatively young (age < 60 years). The coronary MR for siesta of any type was 0.33 (95% CI, 0.14-0.81), which is not very different from that among working men 60 years or older (coronary MR, 0.46; 95% CI, 0.09-2.42).

Table 3. Cox Regression–Derived, Adjusted Coronary Mortality Ratios Among Men by Pattern of Midday Naps and Employment Status*

Taking Midday Naps†	Currently Working (No. of Deaths, 28) (n = 7301)	Currently Not Working (No. of Deaths, 57) (n = 2268)
No	1.00	1.00
Occasionally	0.36 (0.10-1.29)	0.86 (0.30-2.45)
Systematically	0.36 (0.16-0.80)	0.61 (0.32-1.18)
Yes	0.36 (0.16-0.77)	0.64 (0.33-1.21)

*Data are given as mortality ratio (95% confidence interval). Adjusted for age (continuous, expressed in 5-year increments); smoking status (never and ex-smokers, 1-10, 11-20, 21-30, 31-40, > 40 cigarettes per day, ordered); education (≤ 5 y, 6-11 y, 12 y, ≥ 13 y, ordered); body mass index (continuous); waist-hip ratio (category-specific tertiles, ordered); physical activity (category-specific quintiles of resting metabolic rate, hours per day, ordered); and Mediterranean diet score (from 0 to 9, per unit, ordered). At enrollment, participants were free from coronary infarct, angina, stroke, or cancer.

†“No,” persons never taking midday naps; “systematically,” persons who take midday naps at least 3 times per week, with an average duration of each nap of at least 30 minutes; “occasionally,” all other participants (intermediate category); and “yes,” persons taking midday naps occasionally or systematically.

COMMENT

In a large population-based cohort of persons who, at enrollment, were free of medically substantiated CHD, stroke, or cancer and for whom risk factors for CHD, including diet and physical activity, were ascertained in detail, we found that siesta was associated with lower risk of coronary mortality. The inverse association was evident in men, among whom 85 coronary deaths were observed, but it was only marginal among women, among whom 48 coronary deaths were observed. Among men, the inverse association was striking when the analysis was restricted to men who were currently working at enrollment, whereas it was weaker and not significant among men who were not currently working (largely retirees). We interpret our findings as indicating that among healthy adults, siesta, possibly on account of stress-releasing consequences, may reduce coronary mortality. We were unable to undertake a similar analysis among women because there were only 6 deaths among working women.

The hypothesis that taking midday naps may be inversely associated with the incidence of or mortality from CHD was suggested by the ecological association between the prevalence of the siesta habit (high in Mediterranean and certain Central American countries) and mortality from CHD (low in the indicated countries). Several analytical epidemiological studies of variable design have evaluated this association with conflicting results. These studies are haunted by 2 types of powerful confounding: first, those taking midday naps are likely to have lower levels of physical activity, which is a powerful inverse predictor of CHD, and second, persons with a serious condition including CHD or stroke tend to have daytime resting periods, including siesta,⁹ while also being at an increased risk of coronary death. Thus, unconfounded, unbiased, and reasonably precise results re-

quire large, preferably prospective studies in which physical activity has been accurately measured and in which persons with comorbidity, particularly coronary comorbidity, stroke, and cancer were excluded from the study base.

We have found 3 case-control studies in the literature,¹⁻⁴ 2 from Greece and 1 from Costa Rica, evaluating the association of siesta with mortality. The 2 Greek studies reported an inverse association of siesta with acute CHD episodes,¹⁻³ whereas the Costa Rican study, which was larger and more sophisticated, indicated positive associations.⁴ Nevertheless, case-control studies may not be appropriate in investigating the role of siesta in CHD because cases are by definition survivors, which introduces selection bias, and they are also likely to recall siesta patterns colored by their perception of the possible role of the habit in their disease.

Two prospective cohort studies, both from Israel, had investigated the association of siesta with total and cardiovascular mortality (but not exclusively coronary mortality).^{6,8,16-18} Both were well designed and reasonably large (the first^{8,16} included 1859 individuals 50 years and older and the second^{6,17,18} included 455 individuals 70 years and older). Both studies indicated an increased risk of overall and cardiovascular mortality.^{6,8,16} In neither of them, however, was physical activity finely adjusted for, and the exclusion of persons with chronic conditions at enrollment, as undertaken in the first and larger study, led to an attenuation of the associations in this study. Two other cohort studies among the elderly population reported positive associations between daytime sleepiness and mortality, but they did not examine the role, if any, of habitual siesta, nor did they focus on documentably healthy individuals.^{5,7}

Afternoon siesta could affect coronary mortality in opposite ways. In the short term, awakening after a siesta has similar, though milder, effects to those observed after morning awakening. Thus, blood pressure and heart rate are transiently increased, and there are also changes triggered by humoral factors that may collectively affect thrombogenic potential.^{19,20} These changes are likely to increase, at least in the short term, the risk of a coronary attack or death. On the other hand, afternoon siesta in a healthy individual may act as a stress-releasing habit, and there is considerable evidence that stress has both short- and long-term adverse effects on incidence of and mortality from CHD.²¹⁻²³ Thus, an inverse association between siesta among healthy individuals and coronary mortality would not stand in a biological vacuum, although at this stage neither the epidemiological nor the biological evidence is adequate for conclusive inference. Nevertheless, the existence of a stronger inverse association among working men is compatible with the fact that occupational stress is common in many manual and non-manual professions.^{24,25} The sparsity of coronary deaths among working women did not allow us to explicitly assess whether siesta among women has similar beneficial effects to those noted among men.

Advantages of the present investigation are the reliance on a population-based sample; the cohort design; control for most recognized confounding variables; detailed ascertainment of and control for both occupa-

tional and leisure physical activity¹⁰; exclusion from the analysis of persons who at enrollment had reported histories of myocardial infarction, angina pectoris, stroke, or cancer; focus on an outcome (coronary mortality) that is likely to be related to stress-affecting processes¹; and examination of the association among study participants currently not working or working, the latter being more likely to be healthy, as well as to benefit from a stress-releasing activity like siesta. Among the weaknesses of our study are the relatively small number of outcomes (coronary deaths) and the comparatively short follow-up period.

In conclusion, in a large population-based prospective study, we have found that siesta of apparently healthy individuals, and particularly working men, is inversely associated with coronary mortality after controlling for potential confounders, including comorbidity, diet, and physical activity. This is an important finding because the siesta habit is common in many parts of the world, including the Mediterranean region and Central America.

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