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Original Article

Sleep duration and risk of stroke: a dose–response meta-analysis of prospective cohort studies

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ABSTRACT

Objectives: Suboptimal sleep duration has been considered to increase the risk of stroke incidence. Thus we aimed to conduct a dose–response meta-analysis to examine the association between sleep duration and stroke incidence.

Methods: We searched PubMed, Web of science and the Cochrane Library to identify all prospective studies evaluating the association of sleep duration and nonfatal and/or fatal stroke incidence. Then, restricted cubic spline functions and piecewise linear functions were used to evaluate the nonlinear and linear dose–response association between them.

Results: We included a total of 16 prospective studies enrolling 528,653 participants with 12,193 stroke events. Nonlinear dose–response meta-analysis showed a J-shaped association between sleep duration and total stroke with the lowest risk observed with sleeping for 7 h. Considering people sleeping for 7 h as reference, long sleepers had a higher predicted risk of total stroke than short sleepers [the pooled risk ratios (95% confidence intervals): 4 h: 1.17 (0.99–1.38); 5 h: 1.17 (1.00–1.37); 6 h: 1.10 (1.00–1.21); 8 h: 1.17 (1.07–1.28); 9 h: 1.45 (1.23–1.70); 10 h: 1.64 (1.4–1.92); $p_{nonlinearity}<0.001$]. Short sleep durations were only significantly associated with nonfatal stroke and with total stroke in the subgroups of structured interview and non-Asian countries. Additionally, we found a slightly decreased risk of ischemic stroke among short sleepers. For piecewise linear trends, compared to 7 h, every 1-h increment of sleep duration led to an increase of 13% [the pooled risk ratios (95% confidence intervals): 1.13 (1.07–1.20); $p < 0.001$] in risk of total stroke.

Conclusion: Both in nonlinear and piecewise linear dose–response meta-analyses, long sleep duration significantly increased the risk of stroke incidence.

1. Introduction

Stroke is the second-leading cause of death and a leading cause of disability worldwide [1]. The Global Burden of Disease (GBD) 2013 study showed that, in 2013, there were globally almost 25.7 million stroke survivors; over the 1990–2013 period, there was a statistically significant increase in the absolute number of disability adjusted life years (DALYs) due to ischemic stroke (IS), and deaths, survivors and incident events of as a result of both IS and hemorrhagic stroke [2]. Therefore, it is important to look for the risk factors of stroke, especially those that can be ameliorated by modified lifestyles.

Sleep, an important role in human life, takes up approximately one-third of our lifetime. An optimal sleep duration (7–8 h) predicts fewer deaths [3]. In recent decades, suboptimal sleep duration was widely demonstrated to be associated with bad health outcomes such as obesity, diabetes, metabolic syndrome and hypertension which are risk factors of stroke [4–7]. Thus, accumulating epidemiological studies have begun to investigate whether habitual sleep duration is related to stroke. Several primary studies have put forward a curvilinear relationship between sleep duration and stroke [8,9], where both short and long sleep duration led to an increase in

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the risk of stroke. However, discrepancies exist in the literatures that supports this association; some conclude that either short or long sleep duration is associated with stroke [10–13], while others found that a null association exists between them [14–18].

Four meta-analyses found that both short and long sleep duration were significant predictors of stroke [11,19–21], but most of them used a traditional two-category model, which led to massive loss of information for sleep durations in primary studies divided into more than two categories. This we conducted a dose–response meta-analysis based on prospective studies to explore the association between sleep duration and stroke incidence.

2. Materials and methods

We performed this study following the guidelines recommended by the meta-analysis of observational studies in epidemiology (MOOSE) checklist [22].

2.1. Data source and searches

We searched PubMed, Web of Science and the Cochrane Library. PubMed search terms were {[(stroke) or cerebral infarction] or cerebrovascular accident} and sleep duration. Similar search terms were used for Web of Science and the Cochrane Library (for detailed search queries, see Table S1). The search included all relevant studies published before 3 November 2016 with no language limitations. We also screened the reference lists of relevant review articles and included studies for additional information.

2.2. Study selection

We included studies investigating the association of between sleep duration and nonfatal and/or fatal stroke incidence that met the following criteria: (1) the study design was prospective, (2) the population were adults (age > 18 years), (3) the mean or median follow-up duration was more than two years, (4) there were available effect estimates [risk ratio (RR), hazard ratio (HR)], and 95% confidence intervals (CIs) for at least three quantitative categories of sleep duration, (5) subjects had no stroke history at the baseline. Furthermore, if multiple publications were available for a study, we included the report with the longest follow-up.

2.3. Data extraction and quality assessment

Two of our authors extracted the following data independently and in duplicate, using a pre-defined standardized data-extraction form: name of first authors, publication year, country of origin of the population studied, study design, follow-up period, participant characteristics (sex and age), exposure and outcome assessment, sleep duration categories, sample size (numbers of participants and incident cases) in each category, covariates adjusted in the multivariable analysis, and effect size (RRs or HRs) with 95% CI for all categories of sleep duration. When studies had several adjusted models, we extracted those that had the maximum extent of adjustment for potentially confounding variables. The differences between these were resolved through discussion and consensus with another of our authors. We used 'hours' as the common scale of sleep duration.

Quality assessment was performed according to the Newcastle–Ottawa Quality Assessment Scale (NOS), which is a validated scale for non-randomized studies in meta-analyses. The NOS tool contains nine items, four for selection of participants and measurement of exposure, two for comparability of cohorts on the basis of the design or analysis, and three for assessment of outcomes and adequacy of follow-up, and each item is assigned with a star if a study meets the criteria of the item [23]. We considered a study to be of high quality if it scored more than six.

2.4. Statistical analysis

First, we separately summarized the RRs for the shortest and longest sleep duration in each included study compared to its own reference category to explore possible association between sleep duration and total stroke incidence using the random effects meta-analysis [24]. Heterogeneity was evaluated by I^2 and Cochran's Q [25], and it was classified as low (I^2 < 25%), moderate (25% ≤ I^2 < 50%) or high (≥50%) Potential publication bias was evaluated by funnel plots and by Egger's test and Begg's test [26].

For dose–response meta-analysis, considering the log relative risk as an independent variable and the exposure level as a dependent variable, we first adopted restricted cubic splines with five knots at first, 25th, 50th, 75th, and 99th percentiles of exposure distribution in the dose–response meta-regression model to evaluate potential nonlinear trends between sleep duration and total stroke, nonfatal stroke, and fatal stroke [27]. Generalized least-square method was used to estimate the parameters [28,29]. In each of the included studies, we assigned the reported median or mean sleep duration of each category as the category sleep duration. When a study reported only the range of sleep duration for a category, we used the average value of the lower and upper bounds of that category. When the shortest or the longest category was open-ended, we assumed that the open-ended interval length had the same length as the adjacent interval. Additionally, the number of stroke cases and participants (or person-years) of each category of sleep duration was required, and these numbers were inferred based on total number of cases and the reported risk estimates if the study didn't report them [30]. The *p*-value for nonlinearity was calculated by testing the null hypothesis that coefficients of the second, third and fourth spline were zero [29]. Then, we set 7 h as the reference category to predict RRs and 95% CI of stroke under different sleep durations [10]. Finally, if a U-, J- or S-shape or their reverse association was observed, we treat the slope of the curve as two piecewise with a cut point of 7 h to discuss the linear trend on both sides, respectively [31,32].

If the study only reported information by sex, we considered them as two cohorts. All the regression coefficient and results were pooled in a random-effects model to account for heterogeneity among studies [33]. At the same time, we conducted subgroup analyses of nonlinearity and linearity based on stroke subtype, sex, location, the assessment of sleep duration, excluding studies that enrolled special populations because they were considered to be potential residual confounders. Analyses were performed with STATA version 12.0 (StataCorp, College Station, TX) and all tests were two-sided with a significance level of 0.05.

3. Results

3.1. Literature search and study characteristics

A detailed description of how studies were selected is presented in Fig. 1. Briefly, from the preliminary literature search, a total of 825 titles and abstracts were identified. After excluding 786 irrelevant records, we read 39 full-text articles for further assessment. Eventually, we identified 12 articles that met all criteria for this meta-analysis, which enrolled a total of 528653 participants with 12,193 stroke events [10,11,13–17,34–38].

The characteristics and quality score of the individual studies are shown in Table 1. Among 12 included studies, four only reported information on separate sexes [14,17,36,37]. Thus, we eventually had 16 cohorts. The mean or median follow-up duration ranged