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Brief Communication

Sleep quality correlates with the carotid intima-media thickness in stroke-free community-dwelling adults living in rural Ecuador. The Atahualpa Project

Oscar H. Del Brutto [a, *], Robertino M. Mera [b], Mauricio Zambrano [c], Leslie V. Simon [d], Gautam V. Matcha [e], Pablo R. Castillo [f]

[a] School of Medicine, Universidad Espíritu Santo – Ecuador, Guayaquil, Ecuador
[b] Vanderbilt University Medical Center, Nashville, TN, USA
[c] Community Center, The Atahualpa Project, Atahualpa, Ecuador
[d] Emergency Medicine Department, USA
[e] Internal Medicine Department, USA
[f] Sleep Disorders Center, Mayo Clinic School of Medicine, Jacksonville, Fl, USA

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ABSTRACT

Background/Objectives: Evidence of an association between sleep disorders and extracranial atherosclerosis is limited and has not been studied in remote rural settings, where living conditions and cardiovascular risk factors are different than in urban centers. We assessed the relationship between the carotid intima-media thickness (cIMT) and sleep quality in stroke-free individuals aged ≥40 years living in rural Ecuador.

Methods: Applying a population-based study design, participants underwent face-to-face interviews using the Pittsburgh Sleep Quality Index (PSQI) to assess sleep quality, and sonographic examinations for measurement of the carotid intima-media thickness (cIMT). The association between the cIMT and sleep quality (as the dependent variable) was assessed by means of generalized linear models, adjusted for relevant confounders.

Results: The mean age of 561 participants was 60.4 ± 12.6 years (58% women). The mean PSQI was 4.6 ± 2.2 points. Of those, 79 (14%) individuals had an increased cIMT (>1 mm). A model adjusted for demographics showed a significant association between increased cIMT and the PSQI score (β: 0.602; 95% C.I.: 0.027–1.177; $p = 0.040$). This relationship was reduced when cardiovascular risk factors were added to the model (β: 0.514; 95% C.I.: −0.072 – 1.101; $p = 0.086$). When the model was adjusted for demographics and psychological distress, the association between increased cIMT and the PSQI score became significant (β: 0.573; 95% C.I.: 0.013–1.133; $p = 0.045$). In addition, both symptoms of depression ($p = 0.032$) and anxiety ($p < 0.001$) remained independently significant.

Conclusions: This study shows an association between increased cIMT and the PSQI score, which is, at least, partly mediated by manifestations of psychological distress.

1. Introduction

The burden of sleep disorders and cardiovascular diseases is on the rise in most of the developing world [1,2]. It is plausible that a relationship exists between these conditions, explaining their simultaneous increase. In this view, there is evidence suggesting an association between non-breathing sleep-related symptoms and extracranial atherosclerosis [3–10]. However, information is inconsistent and this association has not been studied in rural areas of developing countries, where some features make them unique for assessing specific correlates of these conditions [11]. Preliminary findings from the Atahualpa Project suggest an association between poor sleep quality and cardiovascular risk factors and diseases [12,13]. In this study, we assessed the relationship between the carotid intima-media thickness (cIMT) – used as a surrogate of

* Corresponding author. Air Center 3542, PO Box 522970, Miami, Fl, 33152-2970, USA.
E-mail address: oscardelbrutto@hotmail.com (O.H. Del Brutto).

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extracranial atherosclerosis – and sleep quality in stroke-free individuals aged ≥40 years enrolled in this cohort.

2. Methods

2.1. Study population

Atahualpa is a rural village located in coastal Ecuador. Homogeneity of the population regarding race/ethnicity, living conditions and dietary habits, reduce the risk of unexpected confounders at the time of analyses [14]. The Institutional Review Board of Hospital-Clínica Kennedy, Guayaquil (FWA 00006867) approved the study. Participants signed a comprehensive informed consent form before enrollment.

2.2. Sleep quality assessment

Sleep quality was assessed by the use of the Pittsburgh Sleep Quality Index (PSQI), as detailed elsewhere [15]. The instrument was administered by trained field personnel by means of face-to-face interviews. The PSQI consists of 19 items grouped into seven components, each weighted on a 0 to 3 scale, for a total score of 21 points. Components of the PSQI include assessment of sleep duration, sleep disturbances, sleep latency, daytime dysfunction due to sleepiness, sleep efficiency, overall sleep quality, and medications needed to sleep.

2.3. Carotid B-mode ultrasounds

Exams were performed by the use of a Terason Smart 3300 NexGen ultrasound scanner (Teratech Corporation, Burlington, MA, USA) and a 4–15 MHz linear probe, following a previously defined protocol [16]. To assess the cIMT, we scanned the near and far walls of each carotid artery at three places: (1) the segment extending from 10 to 20 mm proximal to the tip of the flow divider into the CCA, (2) the carotid bifurcation from the tip of the flow divider extending 10 mm proximal to the flow divider tip, and (3) the proximal 10 mm of the internal carotid artery (ICA). The cIMT was calculated as the mean of the 12 measurements (six left and six right). A sonographer, who was blinded to sleep-related symptoms, performed the carotid ultrasounds.

2.4. Confounding variables investigated

Demographics, cardiovascular risk factors and psychological distress were chosen as confounding variables, and were assessed through interviews and procedures previously described in the Atahualpa Project [14]. To assess cardiovascular risk factors, we used the American Heart Association criteria of smoking status, physical activity, diet, body mass index, blood pressure, fasting glucose, and total cholesterol blood levels [17]. Psychological distress was evaluated by the use of the Depression-Anxiety-Stress Scale (DASS-21), a reliable field instrument comprising three sets of questions evaluating symptoms of depression, anxiety and stress [18]. To recognize patients with overt strokes, rural doctors screened all participants with the use of a validated field instrument; neurologists later confirmed the diagnosis with the aid of MRI.

2.5. Statistical analysis

Data analyses were carried out by using STATA version 15 (College Station, TX, USA). In univariate analyses, continuous variables were compared by linear models and categorical variables by the x^2 or Fisher exact test as appropriate. To assess the independent association between the presence of increased cIMT and the PSQI score (as the dependent variable), we fitted generalized linear models, adjusted for demographics, cardiovascular risk factors and manifestations of psychological distress.

3. Results

Of 863 individuals aged ≥40 years enrolled in the Atahualpa Project (2012–2017), 691 were active at the time of the current invitation. The remaining individuals had died, moved out of the village or declined consent. Carotid ultrasound examinations were performed in 594 of 691 individuals (86%); the others refused the to have this study. Of these 594 individuals, 29 were excluded because of an overt stroke as well as four because of motion artifacts precluding evaluation of the cIMT (Fig. 1).

The mean age of the 561 participants was 60.4 ± 12.6 years, and 323 (58%) were women. Twenty (4%) individuals were current smokers; 28 (5%) had a poor diet; 32 (6%) had poor physical activity; 158 (28%) had a body mass index ≥30 kg/m^2; 183 (33%) had blood pressure ≥140/90 mmHg; 149 (27%) had fasting glucose ≥126 mg/dL; and 61 (11%) had total cholesterol levels ≥240 mg/dL. According to the DASS-21 scale, 59 (11%) individuals had symptoms of depression, 81 (14%) had anxiety and 56 (10%) had stress. The mean PSQI was 4.6 ± 2.2 points, with 168 (30%) individuals disclosing a poor sleep quality (PSQI score ≥6 points). The mean cIMT was 0.85 ± 0.17 mm in the entire population, with 79 (14%) individuals having an increased cIMT (mean cIMT >1 mm).

In univariate analyses, individuals with a poor sleep quality had more often poor physical activity ($p = 0.019$), symptoms of depression ($p < 0.001$), anxiety ($p < 0.001$) and stress ($p = 0.018$) than those with a good sleep quality. In addition, there were borderline associations between a poor sleep quality and age ($p = 0.084$) and the mean cIMT ($p = 0.051$). Conversely, an increased cIMT was significantly associated with age ($p < 0.001$), being male ($p < 0.001$), having a poor diet ($p = 0.044$), poor physical activity ($p = 0.032$), blood pressure levels ≥140/90 mmHg ($p < 0.001$), and higher PSQI scores ($p = 0.002$).

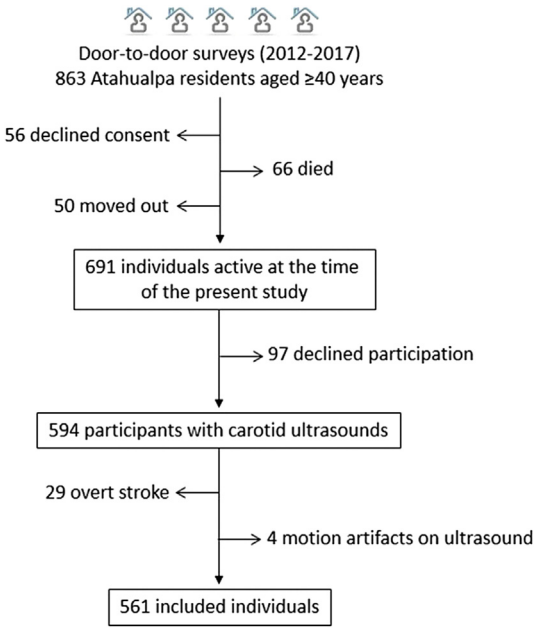

Fig. 1. Flow diagram depicting the process of enrollment and the reasons for not including potentially eligible individuals at each step of the process.

Table 1
Generalized linear models, adjusted for demographics (upper panel), demographics and cardiovascular risk factors (center panel), and demographics and psychological distress (lower panel), fitted to assess the independent association between the Pittsburgh Sleep Quality Index (PSQI) score (as the dependent variable) and the presence of increased carotid intima-media thickness (cIMT).

PSQI score	β coefficient	95% confidence interval	*p* value
Increased cIMT	0.602	0.027 – 1.177	0.040*
Age	−0.014	−0.029 – 0.002	0.091
Sex	0.058	−0.319 – 0.436	0.761
Increased cIMT	0.514	−0.072 – 1.101	0.086
Age	−0.009	−0.027 – 0.008	0.299
Sex	0.016	−0.378 – 0.409	0.937
Smoking	0.029	−0.993 – 1.051	0.955
Body mass index	−0.182	−0.605 – 0.240	0.397
Physical activity	0.334	−0.482 – 1.149	0.422
Diet	0.541	−0.325 – 1.407	0.220
Blood pressure	0.145	−0.276 – 0.566	0.500
Fasting glucose	0.223	−0.202 – 0.648	0.303
Total cholesterol	−0.239	−0.831 – 0.354	0.429
Increased cIMT	0.573	0.013 – 1.133	0.045[a]
Age	−0.013	−0.028 – 0.002	0.100
Sex	0.141	−0.234 – 0.516	1.000
Symptoms of depression	0.727	0.062 – 1.391	0.032[a]
Anxiety	1.194	0.619 – 1.768	<0.001[a]
Stress	−0.166	−0.853 – 0.521	0.636

[a] Statistically significant result.

Table 1 shows results of fitted generalized linear models. A model adjusted for demographics showed a significant association between the presence of increased cIMT and the PSQI score ($p = 0.040$). This relationship was less evident when cardiovascular risk factors were added to the model ($p = 0.086$); none of the investigated cardiovascular risk factors remained independently significant. In contrast, when the model was adjusted for demographics and manifestations of psychological distress, the association between the presence of increased cIMT and the PSQI score became significant ($p = 0.045$). Moreover, both symptoms of depression ($p = 0.032$) and anxiety ($p < 0.001$) remained statistically significant.

4. Discussion

This study shows an association between increased cIMT and the PSQI score in stroke-free community-dwelling adults living in a remote rural setting. This association was partly mediated by manifestations of psychological distress.

As noted, previous studies aiming to investigate the association between extracranial atherosclerosis and non-breathing sleep-related symptoms gave inconsistent results, which were partly related to heterogeneity in study designs. While carotid artery atherosclerosis, has been uniformly assessed by means of the cIMT, evaluation of sleep-related symptoms varied from one study to another. Some studies have focused only on sleep hours [3,5,7] while others have taken into account the quality of sleep, which has been assessed either objectively (actigraphy) or subjectively (the PSQI) [6,8–10]. Furthermore, some studies have not evaluated samples of the population at large, but have been confined to police officers [8], diabetics [9], or women [10]. Most studies have shown associations between sleep hours and the cIMT, which often showed a U-shaped curve, with shorter or longer sleep hours associated with increased cIMT [3,5,7]. In contrast, studies evaluating the association between increased cIMT and poor sleep quality gave more inconsistent results, with some showing a direct association [6,10] while other disclosing no association at all [8].

The relationship between sleep disorders and cardiovascular risk factors and diseases has been extensively studied, but the actual cause of this association is elusive. Pathogenetic mechanisms involved in the association between extracranial atherosclerosis and non-breathing sleep-related symptoms are complex; and are probably related – but not limited – to modifications in inflammatory markers, hormonal factors, lipid metabolism, the effect of the sympathetic nervous system, and endothelial dysfunction [19]. In addition, psychological distress may play a role in this association [20]. Results from our study are in line with this assumption since the association between the cIMT and sleep quality dampened when cardiovascular risk factors were included in the model but became significant when covariables of psychological distress were included.

This study had several limitations. First, we relied on the cIMT, which may not accurately define carotid artery atherosclerosis; however, this measurement has been used by most investigators attempting to assess the burden of this condition in populations [16]. Other limitations are as follows: the cross-sectional design (precluding assessment of causation); the use of subjective assessment of sleep quality; and the fact that Atahualpa residents may not be representative of people living in other villages of the region.

The major strengths of our study include the population-based design as well the unbiased inclusion of a homogeneous population of stroke-free individuals, providing – for the first time – a scenario for studying the association between subclinical atherosclerosis and sleep quality in a remote rural setting. Knowledge of the impact of risk factors involved in this association will help implementation of more informed public health strategies. Thus, application of these strategies may reduce catastrophic consequences of subclinical atherosclerosis in people living in these underserved populations.

Authors' contribution

Oscar H. Del Brutto: study design, manuscript drafting; **Robertino M. Mera**: statistical analyses; **Mauricio Zambrano**: data collection and analysis; **Leslie V. Simon**: significant contribution to intellectual manuscript content; **Gautam Matcha**: ultrasound examinations; **Pablo R. Castillo**: study design, significant contribution to intellectual manuscript content.

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Conflict of interest

The authors have nothing to disclose.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2018.11.017.

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