ORIGINAL ARTICLE: SOCIAL RESEARCH,
PLANNING AND PRACTICE

Sleep complaints are associated with frailty in Mexican older adults in a rural setting

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Aim:　The aim of the present study was to examine the association between sleep complaints and frailty status in a cohort of older adults from rural Mexico, and determine if this association varies according to sex.

Methods:　A cross-sectional study was carried out on a total of 591 community-dwelling adults aged ≥70 years in rural settings of Mexico. Sleep complaints were based on self-reported sleep problems. Frailty status was assessed according to the Fried *et al.* proposal, as well as general health measurements taken from participants. Multivariate logistic regression was used to analyze the association between sleep complaints and frailty.

Results:　Frail participants accounted for 10.7% of the study sample. After adjusting for potential confounders, sleep complaints were associated with increased odds of frailty in women (OR 3.24, 95% CI 1.34–7.84), but not in men (OR 0.76, 95% CI 0.23–2.51).

Conclusions:　In this cohort of rural Mexican older adults, sleep complaints were associated with frailty in older women. Because sleep quality is potentially remediable, future frailty prevention interventions should take sleep complaints into account. **Geriatr Gerontol Int 2017; ••: ••–••**.

Keywords:　aged, frail elderly/statistics and numerical data, independent living, rural population, sleep initiation and maintenance disorders/epidemiology.

Introduction

Sleep disorders constitute a set of symptoms commonly reported in older adults (OA). It has been observed that between 9% and 50% of OA present sleep issues, such as difficulty falling asleep, intermittent wakefulness during the night, shortened total sleep time and/or inefficient sleep.[1]

While the root of sleep disorders is oftentimes secondary to other diseases, comorbidity or symptoms that precipitate or perpetuate them,[1,2] their occurrence has also been identified as a risk factor of cognitive decline or dementia[3] and mortality.[4]

As sleep disorders are believed to rarely occur among healthy OA, their presence is indicative of potential physical declines.[5] Exposure to sleep disorders is related to pathophysiological anomalies including neurohormonal, circadian and homeostatic alterations, such as unstable activity in the adrenal–hypothalamic–pituitary and the hypothalamic–pituitary-gonadal axes; chronic inflammation; and decreased levels of growth hormone and insulin-like growth factor-1.[6] As these conditions are also involved in the pathophysiological mechanisms of frailty, the association between sleep disorders and frailty is not an unexpected outcome.

Frailty is a common geriatric syndrome with a prevalence rate ranging from 4% to 17%, depending on the specific OA population.[7] Its importance stems from its role as a predictor of adverse health events, such as falls, disability and premature death.[8] Therefore, efforts to better understand the determinants of frailty continue to be of primary importance. The study of sleep disorders and their connection with frailty is recent, and is drawing increased attention.

It has been observed that prolonged sleep, insomnia, excessive napping,[9] self-perception of poor sleep quality, reduced sleep efficiency, sleep onset latency, fragmented sleep,[10,11] sleep-disordered breathing[10–12] and daytime

sleepiness[10,13] are all independently associated with the frail phenotype. However, results are inconclusive, and available information either relates specifically to OA in the USA or is confined to male OA. This makes it difficult to generalize outcomes to other ethnic or racial groups, whereas according to some studies, sleep disorders fluctuate with these characteristics,[14] and are particularly common among low- and middle-income countries.[15]

The pathophysiological mechanisms of sleep disorders and frailty suggest a bidirectional relationship; notwithstanding, most epidemiological studies place sleep disorders specifically as a risk factor for frailty. Although both conditions are reversible, it has been proposed that studying sleep as a risk factor for frailty has more practical clinical implications.[16] Based on this guideline, the present study sought to assess whether or not sleep disorders were associated with the frailty phenotype in a cohort of rural Mexican OA aged ≥70 years.

Methods

Sample and procedures

We used data from the Rural Frailty Study, a prospective study designed to estimate the prevalence of frailty in rural settings in Mexico. Baseline measurement of the study was carried out in 2009, and the first follow-up measurement in 2013. The latter provided data for the present study. Details of the Rural Frailty Study have been reported elsewhere.[17] Briefly, at baseline, the study sample consisted of 600 OA. This sample size was calculated to detect prevalence rates of at least 4%, with 80% statistical power and 5% significance level. During follow up, 668 completed interviews were achieved: 495 follow-up and 173 new sample interviews. The response rate during follow up was 89%. Interviews were administered to target individuals or to proxy informants where participants were found to have died. The study was approved by the ethics committee of the National Institute of Public Health, and written informed consent was obtained from all participants.

Measures

Definition of frailty

The frailty phenotype was determined according to the Fried proposal.[8] Its composite measure was defined as follows. (i) Slow gait speed: gait speed was evaluated by the time taken to walk a 4-m walking test. The cut-off point in our population was adjusted for sex and height, and based in the worst quintile, participants in this quintile were identified as having slow gait speed. (ii) Poor handgrip strength: grip strength (kg) was measured using a hand dynamometer (Baseline Electronic Smedley Hand Dynamometer, Fabrication Enterprises, White Plains, NY, USA). Three measurements were made in both

hands, and the highest one of all was considered. The cut-off point in our population was adjusted for body mass index (kg/m^2) and sex, and was based in the worst quintile. (iii) Low physical activity level: defined using the short form of the International Physical Activity Questionnaire, which collects physical activity participation in hours and minutes.[18] Using the International Physical Activity Questionnaire guidelines, a continuous score expressed in Metabolic Equivalent of Task min/week was calculated. This continuous score was converted to a weekly energy expenditure in kilocalories. The criteria for low physical activity was based in the worst quintile adjusted for sex. (iv) Exhaustion: participants with a negative response to the following two questions from the Geriatric Depression Scale were considered to be exhausted: "Do you feel full of energy?" and "Do you have enough energy for your everyday life?" (v) Weight loss: weight loss was defined as a self-reported, unintentional weight loss of ≥5 kg in the 6 months before the interview. Participants who responded positively were classified as frail for this component.

Respondents were considered frail if they met three or more, prefrail if they met one or two and not-frail or robust if they met none of the above criteria.

Sleep complaints

Participants responding "yes" to the following question were identified as having sleep complaints: "Have you had trouble sleeping recently?" The same question had been previously used during the 10/66 Dementia Research Group study.[15]

Covariates

The following covariates were used: sex, age, literacy (self-reported ability to read and write), ethnicity (self-reported use of an indigenous language), labor status (engaging in a paid job) and marital status (being married/living in a common-law relationship *vs* not having a partner). For disability, we used the Katz scale[19] to assess difficulties in basic activities of daily living (ADL), which include bathing, dressing, toileting, transferring, continence and feeding. We also used the Lawton scale[20] to assess difficulties in instrumental ADL (IADL): using the telephone, going shopping, managing drugs and money, using public or private transportation and, for women, preparing meals as well as doing housekeeping and laundry. Participants who reported requiring help or being unable to carry out at least one of the preceding activities were considered disabled for ADL or IADL.

Participants were also asked whether they had been diagnosed by a physician with any of the following eight chronic diseases: hypertension, diabetes, hypercholesterolemia, coronary heart disease, stroke, chronic pulmonary obstructive disease, arthritis and osteoporosis. Each self-reported disease was added up

using a score from 0 to 8, with higher scores indicating a larger number of chronic diseases.

Use of medications was assessed in relation to the eight aforementioned diseases; the number of medications used was assigned a value from 0 to 8, with higher values reflecting increased consumption of medications. To assess cognitive impairment, we used the subjective memory complaint through the question "Have you had any difficulty with your memory?", which was operationalized as a binary variable.

The Short Physical Performance Battery is a standardized measure of lower extremity physical performance involving three dedicated physical performance activities: walking gait, balance and ability to rise from a chair. Short Physical Performance Battery scores range from 0 to 12 points, with lower scores reflecting poorer lower extremity function levels.[21] Lower extremity physical performance was used as a categorical variable (<8 points represented worse lower extremity performance).

Analytical sample

The present study analyzed a sample of 591 adults aged ≥70 years. From the original sample of 668 participants, 77 were excluded as a result of incomplete data regarding either the frailty phenotype or covariates. Excluded participants were mostly illiterate, frailer, had more ADL/IADL disabilities, poorer lower extremity function levels and poorer cognitive performance. No statistical differences were observed in the remaining study variables.

Statistical analysis

Variables were described using either arithmetic means or proportions, as appropriate. In bivariate analysis, the following statistical procedures were used according to the characteristics of each variable: the χ^2-test for categorical data and the Kruskal–Wallis test for continuous data. The association between sleep complaints and frailty was estimated using a binary logistic regression model. Furthermore, to investigate if there was a heterogeneous association between sleep complaints and frailty, according to the sex of OA, we added an interaction term of sex by sleep complaints in the logistic regression model. The model was evaluated in regard to collinearity, goodness of fit and residuals. Differences were considered statistically significant where $P < 0.05$ and 95% confidence intervals (CI) were given. All data were analyzed using Stata 13.0 software (StataCorp LP, College Station, TC, USA).

Results

The mean age was 76.3 ± 3.3 years, 52.8% were women, 38% were literate and 48.6% had a partner (married or in common-law). Of the 591 older adults from rural Mexico, 10.7% ($n = 63$) were classified as frail, 51.9% ($n = 307$) were prefrail and 37.4% ($n = 221$) were non-frail. The global prevalence of sleep complaints was 20.0% (21.8% in women, 16.8% in men). Frail Mexican older adults had more complications than non-frail or prefrail ($P < 0.05$); however, sleep complaints did not differ between the non-frail and prefrail group. Characteristics of the entire study population and characteristics according to frailty status are shown in Table 1.

For covariates, in comparison with the non-frail group, frail individuals were more likely to be unemployed ($P < 0.01$), had more subjective memory complaint ($P < 0.05$), were older ($P < 0.01$), had higher dependence in IADL ($P < 0.001$) and ADL ($P < 0.001$), had low physical performance ($P < 0.001$), and took a higher

Table 1 Demographic and health characteristics of older adults by frailty status in rural Mexico

	Non-frail 221 (37.4%)	Prefrail 307 (51.9%)	Frail 63 (10.7%)	P-value
Sleep complaints (%)	17.2	18.6	31.8	0.031
Women (%)	51.6	53.1	55.6	0.846
Ethnicity (%)	33.5	40.1	39.7	0.285
Literacy (%)	45.3	33.6	34.9	0.021
Paid job (%)	42.5	24.1	7.9	0.000
With partner (%)	50.7	48.5	41.3	0.419
Subjective memory complaint (%)	27.6	30.6	44.4	0.038
ADL disability (%)	7.7	18.9	57.1	0.000
IADL disability(%)	16.3	26.4	61.9	0.000
SPPB, <8 (%)	17.2	37.5	82.5	0.000
Mean number of medications	0.45	0.63	0.79	0.006
Mean age (years)	75.6	76.5	77.4	0.000
Mean number of diseases	0.81	1.00	1.14	0.017

ADL, basic activities of daily living; IADL, instrumental activities of daily living; SPPB, Short Physical Performance Battery.

number of medications ($P < 0.01$). It is also noticeable that subjective memory complaint, the prevalence of ADL disability and IADL disability, and low Short Physical Performance Battery increased across the frailty status group. However, no significant differences were observed regarding sex, ethnicity and married status between the three groups of frailty.

Table 2 shows the results of the logistic regression model. Significant associations were observed for ADL disability (OR 2.65, $P < 0.05$) and physical performance (OR 6.84, $P < 0.01$), both variables increasing the likelihood of being frail. As for the association between frailty and sleep complaints, we found a significant interaction term between sex and sleep complaints. For men there was no association (OR 0.77, $P = 0.668$), but for women the presence of sleep complaints rose the odds of being frail (OR 3.20, $P < 0.01$). In fact, the probability of being frail tripled among women with sleep complaints as compared with those without (Fig. 1).

Discussion

In our sample of OA aged ≥70 years, the likelihood of the frailty phenotype in women rose threefold with the presence of sleep complaints. The present findings match those of other epidemiological (cross-sectional and prospective) studies where various indicators of sleep disorders and sleep quality were found to pose significant functionality risks and were strongly correlated with frailty.

Previous studies have reported that daytime sleepiness and sleep duration are associated with the presence and incidence of frailty.[9,13] Regarding Latin America, for instance, one study observed that poor sleep quality and sleep onset latency were associated with frailty among institutionalized OA in Brazil.[22] Another Brazilian study
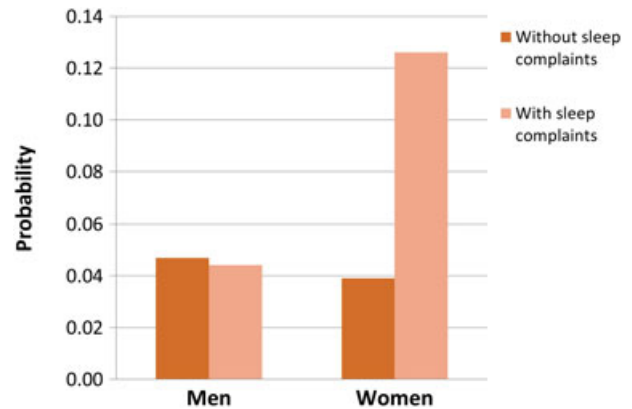
Figure 1 Probability of experiencing frailty by sleep complaints and sex in rural Mexico.

found that individuals with diminished physical activity showed a greater presence of sleep disturbances – specifically in regard to the number of naps per week – than those without (6.1 *vs* 5.8, respectively, $P < 0.05$).[23] Finally, 34% of participants in a sample of 311 rural community OA aged ≥60 years in Ecuador reported poor sleep quality according to the Pittsburgh sleep scale, a condition that was found to correlate with increased frailty according to the Edmonton frailty scale (β = 0.23, 95% CI 0.11–0.35).[24]

Sleep disorders negatively affect hormonal and metabolic functions by shortening the delta sleep phase (or deep sleep phase), which, in turn, reduces growth hormone secretion and promotes cortisol secretion.[6] Lower growth hormone levels contribute to a decline in muscular mass, and strength, higher cortisol levels and a higher cortisol : dehydroepiandrosterone sulphate ratio contribute to a decline in physical function, three elements that have been linked to the development of sarcopenia and frailty.[25]

Table 2 Logistic regression model for factors associated with frailty in rural Mexico

Variables	Odds ratio	95% confidence interval	*P*-value
Sleep complaints by sex			
Men	0.77	0.23–2.55	0.668
Women	3.20	1.33–7.68	0.009
Age	1.03	0.94–1.13	0.515
Ethnicity	1.70	0.88–3.30	0.115
Literacy	1.48	0.75–2.90	0.258
Paid job	0.40	0.14–1.16	0.093
With partner	0.78	0.38–1.60	0.496
Number of diseases	0.64	0.40–1.01	0.058
Subjective memory complaint	1.20	0.63–2.27	0.585
Number of medications	1.64	0.91–2.95	0.099
ADL disability	2.65	1.27–5.52	0.010
IADL disability	1.72	0.82–3.58	0.150
SPPB (<8)	6.84	3.08–15.20	0.000

ADL, basic activities of daily living; IADL, instrumental activities of daily living; SPPB, Short Physical Performance Battery.

As for the conditional relevance of sex, in an analytical sample of 1042 OA (aged 77 years on average) pertaining to the Cardiovascular Health Study, sex differences were observed in the association between sleep disorders and frailty.[12] Based on the Fried frailty phenotype, the study found that sleep apnea was associated with one or more frailty components in women (OR 4.85, 95% CI 1.40–16.78), but not in men (OR 1.08, 95% CI 0.58–2.00). It was specifically associated with two frailty components: slow walking gait and diminished grip strength.

The plausibility of a differential association between men and women is based on the fact that women experience more physiological disruption and greater vulnerability to stress than men. A recent systematic review showed that systemic inflammation provoked by sleep deprivation, insomnia and poor sleep quality varies with sex.[26] Women tend to show higher C-reactive protein (CRP) and interleukin-6 levels; increased Toll-4 type receptors linked to the production of monocytes and inflammatory cytokines; and overactivation of nuclear factor κB – all of which act as markers in the pathogenesis of frailty. Prospective epidemiological studies of OA have confirmed that high concentrations of C-reactive protein and fibrinogen predict frailty incidence in women more than in men.[27] Furthermore, low dehydroepiandrosterone levels can render women more vulnerable to the effects of sleep disorders and frailty, although results on the correlation between dehydroepiandrosterone and frailty modulated by sex are less conclusive.[28]

Previous studies have documented that a low physical performance is an early indicator of frailty, even in high-functioning OA.[29] We also found a strong association, but it is remarkable that in the present study the group of frail OA was composed of a high proportion of individuals with lower physical performance than the groups of robust and prefrail OA. It could be explained by the inclusion of participants aged ≥70 years. In contrast, the rural population in the present study faces both poverty and lower levels of education, both of which are linked to poor functioning, which is a possible mechanism that leads to frailty. In addition, Mexican OA in rural settings are much more likely to still be engaged in agricultural activities that demand a high metabolic expenditure, which combined with a history of low diet quality (proteins and micronutrients) might explain low physical performance.[30]

Among the most important limitations to the present study is the fact that its cross-sectional design does not allow for drawing conclusions about the direction of causality. The relationship between sleep disorders and frailty can be bidirectional; individuals with sleep disorders are more likely to show medical problems and vice versa. Longitudinal studies are required to validate our results. Furthermore, the fact that our measurement of sleep disorders was based on a self-report of a general indicator

might be considered a limitation. Future studies should consider adding objective measures to complete and discriminate among the circumstances associated with sleep disorders. Finally, we could not assess the use of hypnotics. Hypnotics medications can impact negatively on physical function, which could potentially contribute to an increase in frailty or exacerbate/maintain existing sleep complaints.

Nevertheless, we consider the present study to be of value in that the association between sleep complaints and frailty – predominantly in women – had not been previously reported among rural residents. Additionally, we assessed frailty according to Fried's phenotype proposal, a framework that has been used by few studies to evaluate frailty among rural populations.

Given the paucity of available results on this matter and the escalating need to address frailty in all contexts, the present study provides useful knowledge regarding the risk profile differential between sleep complaints and frailty. This is of particular clinical relevance given that sleep complaints offer a means for identifying those who are vulnerable to frailty. In particular, the present findings have implications for clinical interventions, where understanding the causes of sleep complaints could prevent or delay conversion to frailty.

Acknowledgements

Disclosure statement

The authors declare no conflict of interest.

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