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A Reappraisal on the Associations between Sleep-disordered Breathing, Insomnia, and Cardiometabolic Risk

To the Editor:

Sleep-disordered breathing (SDB) and insomnia are highly prevalent conditions in general population and exhibit significant and independent associations with cardiometabolic risk (e.g., hypertension [HT] and diabetes [DM]) (1, 2). The major effort to define the incremental risk has been directed to SDB or insomnia as isolated conditions, even though both can frequently cooccur. Indeed, comorbid insomnia and sleep apnea (COMISA) has recently emerged as a topic of significant interest (3), whereby despite the obvious clinical divergence of the cardinal symptoms and signs of each of these entities, the two sleep disorders share many common symptoms, which may hinder recognition, diagnosis, and treatment, and hamper the adequate management of patients with COMISA (4).

The hypothesis has been put forth of mutually interactive, bidirectional effects between insomnia and SDB, in which the adverse consequences of COMISA will be enhanced, particularly regarding the cardiovascular system (5, 6). In addition, alterations in the circadian timing system may also interfere with the mechanisms underlying COMISA-associated end-organ morbidities and ultimately potentiate such risks (7–9).

In this context, we eagerly read the recent paper by Li and colleagues (10), which prospectively confirmed the associations between SDB and insomnia with incident HT and DM in U.S. Hispanic/Latino subjects. Because this particular sector of the U.S. population has been recognized as carrying a higher risk of sleep disorders and cardiometabolic disorders, the assumption that sleep perturbations are a modifiable target for disease prevention or risk reduction is particularly attractive and clinically relevant. However, in their study, the authors did not address the potentially increased risk of SDB and insomnia when both of these conditions are present, as in patients with COMISA. Such exercise would be of importance for characterizing the broader spectrum of interactions between these highly prevalent conditions and potentially define a subgroup at higher cardiovascular or metabolic risk.

Accordingly, we recently explored the association between isolated insomnia, isolated SDB, and COMISA and the risk of HT and DM in a retrospective cross-sectional study involving 685 individuals from an initial pool of 758 patients referred to a sleep laboratory in Salvador, Bahia, from October 2014 to October 2018. All medical records contained information on age, sex, height, weight, and body mass index, time to sleep, time to wake up, total sleep time, and the responses to the Epworth Sleepiness Scale and the STOP-BANG questionnaire score. Insomnia was assumed by at least a positive answer to the questions "Do you have difficulty falling asleep?" and "Do you have difficulties maintaining your sleep?" plus identification of the period (beginning, middle, or end of the night) and duration of such symptoms. In addition, for a patient to be considered as having insomnia, he/she should present with at least one daytime consequence, such as fatigue, inability to concentrate, or irritability. To potentiate the risk estimation, we excluded those patients with presumed mild risk for SDB according to the STOP-BANG scores (fewer than two positive answers). COMISA was considered as present when the individual presented a condition compatible with insomnia as well as with moderate/severe risk for SDB according to the STOP-BANG questionnaire (three or more positive answers). Table 1 shows the characteristics of all groups.

The relative frequencies of HT and DM were significantly higher in the COMISA group (54.3% and 13.3%) compared with the isolated SDB (41.9% and 10.1%) or the isolated insomnia group (10.1% and 1.8%) ($P < 0.001$). Excessive diurnal sleepiness scores were higher in the COMISA and SDB groups when compared with the insomnia group (Table 1). Significant reductions in daily total sleep duration emerged in the COMISA group compared with the SDB and insomnia groups ($P = 0.001$), which could independently, or via interactions with the circadian timing system, influence several cardiometabolic outcomes (8, 9). Also, the trend toward later sleep-onset times in the COMISA group may also operate as an important cardiometabolic risk factor (11).

Thus, our findings not only corroborate those of Li and collaborators (10) in another cohort, whereby SDB and insomnia appear to contribute to cardiovascular and metabolic risk, but also expand on such findings and reveal the potentiation of these adverse consequences when both are concurrently present as in patients with COMISA. Further studies examining the underlying mechanisms contributing to this enhanced risk appear warranted. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Originally Published in Press as DOI: 10.1164/rccm.202102-0337LE on March 19, 2021

Table 1. Comparison of Characteristics among the Moderate/High Risk Groups for COMISA, OSA, and Insomnia

Variable	COMISA (*n* = *173*)	OSA (*n* = *322*)	Insomnia (*n* = *168*)	*P* Value
Sex, M, *n* (%)*	98 (54.7)	210 (65.2)	49 (26.6)	<0.0001
Age, yr†				
Median (interquartile range)	51 (39–60)	50 (37–60)‡	36 (31–52)§	<0.0001
Mean ± SD	49.8 ± 13.8	48.5 ± 14.8‡	41 ± 13.8§	
BMI, kg/m²†				
Median (interquartile range)	30 (25–35)	29 (26–34)‡	25 (23–27)§	<0.0001
Mean ± SD	31 ± 6.3	30.8 ± 6.5‡	25.3 ± 3.8§	
Neck circumference, cm†				
Median (interquartile range)	44 (37–50)	42 (37–48)‡	34 (31–38)§	<0.0001
Mean ± SD	44.2 ± 8.9	44.2 ± 9.1‡	35.2 ± 5.5§	
Epworth scale score†				
Median (interquartile range)	10 (5–14)‖	11 (7–16)‡	8 (5–13)	<0.0001
Mean ± SD	10.4 ± 6.8‖	11.9 ± 6.2‡	10.2 ± 6.6	
SAH, *n* %*	94 (54.3)	135 (41.9)	17 (10.1)	<0.0001
Diabetes, *n* (%)*	23 (13.3)	35 (10.9)	3 (1.8)	<0.0001
Uses caffeine, *n* (%)*	113 (63.1)	212 (65.8)	96 (52.2)	0.009
Smoker, *n* (%)*	15 (8.4)	15 (4.7)	4 (2.2)	0.023
Uses alcoholic beverages, *n* (%)*	84 (46.9)	170 (52.8)	75 (40.8)	0.032
Practices physical activity, *n* (%)*	71 (39.7)	137 (42.5)	78 (42.4)	0.804
Time to go to bed, median (interquartile range), h†	23:00 (22:30–00:00)‖	23:00 (22:00–23:30)	23:00 (22:00–23:30)	<0.0001
Wake-up time, median (interquartile range), h†	6:00 (5:00–7:00)	6:00 (5:30–6:30)‡	6:00 (5:30–7:00)	0.009
Total sleep time, median (interquartile range), h†	7:00 (6:00–8:00)‖	7:10 (6:30–8:00)	7:15 (6:30–8:00)§	0.001

Definition of abbreviations: BMI = body mass index; COMISA = comorbid insomnia and sleep apnea; OSA = obstructive sleep apnea; SAH = systemic arterial hypertension.
*Simple and relative frequencies.
†ANOVA or Kruskal-Wallis (Bonferroni) tests.
‡OSA versus insomnia: $P < 0.005$.
§COMISA versus insomnia: $P < 0.005$.
‖COMISA versus OSA: $P < 0.005$.

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