

## Insomnia and cardiovascular outcomes

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Insomnia and cardiovascular diseases (CVD) are 2 disorders that have been intensely discussed in the literature due to their prevalence in the world. Chronic insomnia affects 7 to 15% of the adult population<sup>1,2</sup>, while CVD have been the number one cause of death globally for several years<sup>3</sup>. Many factors contribute to the high prevalence of both disorders, including the classical cardiovascular risk factors<sup>4</sup>, and the predisposition of some individuals to develop insomnia<sup>2</sup>. However, changes in modern society, such as increasing work pressure and the introduction of new technologies have resulted in an increase in stress and sleep deprivation. These both factors can have a negative influence on insomnia and cardiovascular health.

Vgontzas et al. (2009)<sup>5</sup> first reported a link between short sleep duration and CVD and metabolic consequences among individuals with insomnia. In fact, the impact of sleep deprivation on CVD has been well demonstrated<sup>6</sup>. Chronic severe insomnia is associated with hyperarousal and short sleep duration, potentially leading to: 1) hypercortisolemia and increased adrenocorticotropic hormone (ACTH)<sup>5</sup>; 2) increased sympathetic nervous activity, as shown by high levels of norepinephrine and variability in the heart rate of patients with insomnia<sup>7</sup>; and 3) vascular endothelial dysfunction, as indicated by lower flow-mediated dilatation in patients with insomnia<sup>8</sup>. These alterations directly affect cardiovascular function, enhancing the long-term risk of hypertension, coronary disease, and heart failure<sup>7</sup>. Together, short sleep duration (<5h) and insomnia increase the risk of hypertension<sup>5</sup>. Additionally, patients with insomnia have a 45% higher risk of developing CVD. Results from a meta-analysis study have confirmed the importance of insomnia in relation to cardiovascular disease and mortality<sup>9</sup>.

Another important link between these 2 conditions, as described in the review article by Nobre et al. (2021)<sup>10</sup> is the association between insomnia phenotypes, circadian misalignment, and cardiovascular risk. The authors hypothesized that a putative autonomic nervous system imbalance could play a role in this association. This is a plausible hypothesis, as some patients with severe insomnia associated with hyperarousal have been shown to display a nocturnal non-dipping blood pressure profile<sup>11,12</sup>. Other studies have reported high sympathetic activity among patients with chronic insomnia<sup>7</sup>.

In addition to hyperarousal and sleep deprivation, insomnia is related with high levels of anxiety symptoms and stress, which contribute to the incidence of mental and affective disorders<sup>1,13</sup>. One of the most studied mental disorders – depression – has been extensively investigated in cardiovascular research because, as stated by American Heart Association, this disorder worsens the prognosis of patients with CVD<sup>14</sup>. Although the mechanisms linking depression and CVD are not well elucidated, it seems that endothelial dysfunction may occur in patients with depressive symptoms<sup>15</sup>.

Finally, Nobre et al. (2021)<sup>10</sup> raised a very interesting issue in their review of the potential role of circadian misalignment in the pathophysiology of cardiovascular consequences among some insomnia patients. Of note, men with insomnia and difficulty initiating sleep have a higher risk of cardiovascular mortality<sup>16,17</sup>. Insomnia symptoms affect daily routine, increase anxiety and stress, predicting mental disorders, and CVD.

CVD have been a serious public health issue, and it is important to recognize insomnia as one of the main factors indicating a poor prognosis in patients with CVD, and ensure its treatment in order to prevent both insomnia and CVD.

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## REFERENCES

1. Castro LS, Poyares D, Leger D, Bittencourt L, Tufik S. Objective prevalence of insomnia in the São Paulo, Brazil epidemiologic sleep study. *Ann Neurol*. 2013 Oct;74(4):537-46.
2. Kalmbach DA, Anderson JR, Drake CL. The impact of stress on sleep: pathogenic sleep reactivity as a vulnerability to insomnia and circadian disorders. *J Sleep Res*. 2018 Dec;27(6):e12710.
3. World Health Organization (WHO). Cardiovascular diseases (CVDs). Geneva: WHO.
4. Foraker RE, Benziger CP, DeBarmore BM, Cené CW, Loustalot F, Khan Y, et al. Achieving optimal population cardiovascular health requires an interdisciplinary team and a learning healthcare system: a scientific statement from the American Heart Association. *Circulation*. 2021 Jan;143(2):e9-e18.
5. Vgontzas NA, Liao D, Bixler EO, Chrousos GP, Vela-Bueno A. Insomnia with objective sleep duration is associated with a high risk for hypertension. *Sleep*. 2009 Apr;32(4):491-7.
6. Tufik S, Andersen ML, Bittencourt LR, Mello MTD. Paradoxical sleep deprivation: neurochemical, hormonal and behavioral alterations. Evidence from 30 years of research. *An Acad Bras Ciênc*. 2009 Sep;81(3):521-38.
7. Javaheri S, Redline S. Insomnia and risk of cardiovascular disease. *Chest*. 2017 Aug;152(2):435-44.
8. Routledge FS, Dunbar SB, Higgins M, Rogers AE, Feeley C, Ioachimescu O, et al. Insomnia symptoms are associated with abnormal endothelial function. *J Cardiovasc Nurs*. 2017 Jan/Feb;32(1):78-85.
9. Sofi F, Cesari F, Casini A, Macchi C, Abbate R, Gensini GF. Insomnia and risk of cardiovascular disease: a meta-analysis. *Eur J Prev Cardiol*. 2014 Jan;21(1):57-64.
10. Nobre B, Rocha I, Morin CM, Meira e Cruz M. Insomnia and circadian misalignment: an underexplored interaction towards metabolic risk. *Sleep Sci*. 2021;14(1):1-9.
11. Lanfranchi PA, Pennestri MH, Fradette L, Dumont M, Morin CM, Montplaisir J. Nighttime blood pressure in normotensive subjects with chronic insomnia: implications for cardiovascular risk. *Sleep*. 2009 Jun;32(6):760-6.
12. Lyu B, Hagen EW, Ravelo LA, Peppard PE. Blood pressure dipping and sleep quality in the Wisconsin sleep cohort. *J Hypertens*. 2020 Mar;38(3):448-55.
13. Baglioni C, Spiegelhalter K, Nissen C, Riemann D. Clinical implications of the causal relationship between insomnia and depression: how individually tailored treatment of sleeping difficulties could prevent the onset of depression. *EPMA J*. 2011 Sep;2(3):287-93.
14. Lichtman JH, Froelicher ES, Blumenthal JA, Carney RM, Doering LV, Frasure-Smith N, et al. Depression as a risk factor for poor prognosis among patients with acute coronary syndrome: systematic review and recommendations: a scientific statement from the American Heart Association. *Circulation*. 2014 Mar;129(12):1350-69.
15. Sherwood A, Hinderliter AL, Watkins LL, Waugh RA, Blumenthal JA. Impaired endothelial function in coronary heart disease patients with depressive symptomatology. *J Am Coll Cardiol*. 2005 Aug;46(4):656-9.
16. Mallon L, Broman JE, Hetta J. Sleep complaints predict coronary artery disease mortality in males: a 12-year follow-up study of a middle-aged Swedish population. *J Intern Med*. 2002 Mar;251(3):207-16.
17. Fernandez-Mendoza J, He F, Vgontzas AN, Liao D, Bixler EO. Interplay of objective sleep duration and cardiovascular and cerebrovascular diseases on cause-specific mortality. *J Am Heart Assoc*. 2019 Oct;8(20):e013043.