

Possible link between sleep-disordered breathing and cardiovascular disease revealed

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Doctors have long known that snoring is hazardous to health for a number of reasons. In addition to restless nights and increased daytime sleepiness, sleep-disordered breathing (SDB) has a series of associated health problems, including increased risk of cardiovascular disease (CVD). While it is not always clear what the association between SDB and a given health problem is, new research exposes that at least one factor may help to explain the increased risk of cardiovascular problems that affects even people with mild to moderate SDB.

Researcher Reena Mehra, M.D., M.S., assistant professor of medicine at the Case Western Reserve School of Medicine in Cleveland, Ohio, and colleagues set out to investigate the morning and evening levels of three pro-thrombotic markers, plasminogen activator inhibitor-1 (PAI-1), fibrinogen and D-dimer, relative to the severity of SDB as defined by the apnea/hypopnea index (AHI) in 537 subjects.

The study appears online ahead of the print edition of the <u>American Journal of Respiratory and Critical Care</u> *Medicine* on the American Thoracic Society's Web site.

After controlling for variables including <u>body mass index</u> (BMI), age, sex and co-morbidities, they found that for every 5-unit increase in AHI under 15, there was a corresponding significant increase of about 10 percent in PAI-1. Similarly, for every 5-unit increase in AHI under 15,



fibrinogen significantly increased on average by about 8.4 mg/dL. There was no significant increase in D-dimer in relation to AHI, however.

"These data suggest that individuals with even modest levels of SDB (which describes a large proportion of the adult population) may have an enhanced pro-thrombotic biochemical profile, increasing their CVD risk," said Dr. Mehra.

Increased morning PAI-1 remained significantly associated with SDB severity in those with mild to moderate SDB even after taking into account evening PAI-1, suggesting that morning may be a reflection of overnight SDB-related physiologic stress, and indicating that PAI-1 may be a good biomarker for assessing SDB stress. These diurnal findings were not noted with fibrinogen.

Interestingly, there was no association between either PAI-1 or fibrinogen at AHI above 15, which is generally the clinical cut-off between moderate and more sever SDB. "These data suggest that even at levels of SDB considered to be mild, there is an enhanced thrombotic state. Further research is needed to identify whether treatment of milder degree of SDB results in improvements in markers of thrombosis, a known contributor to <u>cardiovascular disease</u>," said Dr. Mehra.

"In summary, these data suggest that, at low to modest levels of SDB, incremental increases in AHI are associated with increases in levels of two pro-thrombotic biomarkers associated with CVD. Future directions include exploring whether treatment of even mild to moderate levels of SDB improves biomarkers of thrombosis, and performing further work to understand the specific pathways and pathobiology of SDB-related increased risk of thrombosis."

John Heffner, M.D., past president of the American Thoracic Society, commented, "This study joins so many others that paint a consistent



picture of sleep as a fundamentally important physiologic process for health that can negatively impact multiple organ systems when disordered breathing occurs. This study provides an important insight into how sleep disruptions can trigger prothrombotic processes that may eventually lead to cardiovascular diseases and perhaps other conditions like strokes. Other investigators will now pursue the interaction of SDB with prothrombic states."

Provided by American Thoracic Society

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