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Title: Periodic limb movements during sleep reflect hypercoagulability in obstructive sleep apnea patients

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Body: Background: Both periodic limb movements during sleep (PLMS) and obstructive sleep apnea (OSA) are major causes of sleep disorders and are reported to be associated with cardiovascular diseases (CVD). However, whether the combination of PLMS and OSA promotes a greater risk of CVD than each condition alone is uncertain. Objectives: To investigate whether patients with both PLMS and OSA have a more elevated hypercoagulability than those with OSA only by examining plasma fibrinogen levels. Methods: Plasma fibrinogen levels were measured in 254 patients who had moderate to severe OSA revealed by diagnostic polysomnography. Results: In 46 (18%) of 254 patients, PLMS were found. Fibrinogen levels were significantly higher in patients with both PLMS and OSA than in those with OSA only (298.2 ± 76.1 vs. 270.0 ± 52.6 mg/dL, $p < 0.01$) while the apnea hypopnea index was significantly lower (33.7 ± 15.1 vs. 40.8 ± 19.9 /h, $p = 0.02$). When the cohort was categorized into two groups based on the plasma fibrinogen level, multivariate analysis revealed that both the 3% oxygen desaturation index (OR, 1.021; 95%CI, 1.006-1.037; $p = 0.007$) and presence of PLMS (OR, 2.698; 95%CI, 1.287-5.884; $p = 0.008$) were potent factors associated with higher fibrinogen levels independently of other confounding factors. Conclusion: PLMS were positively associated with plasma fibrinogen levels in OSA patients. Since the plasma fibrinogen level is an established predictive factor of future CVD events, PLMS can be a useful clinical sign to identify OSA patients with high risk of CVD.