

Sleep apnea can contribute to recurring pulmonary embolism

December 7 2016

Pulmonary embolism (PE) is a major risk for patients suffering from venous thromboembolism (VTE) and can often be fatal. While advanced age, lack of exercise, and obesity all contribute to PE, it has been hypothesized that obstructive sleep apnea (OSA) may also promote the formation of blood clots. Because VTE is a chronic condition with reoccurring episodes of PE, researchers wanted to examine how OSA affected the rate of repeat PE occurrence. They found that after the first PE, OSA increases the risk for PE recurrence. Their results are published in the December issue of *CHEST*.

Patients who have had one PE have a 30% chance of having another episode and recurring PE carries a 9% mortality rate. While anticoagulants are very effective at decreasing the possibility of PE, their use comes with an increased risk of bleeding. Identifying and understanding contributing <u>risk factors</u> that can be managed may help decrease the need for blood thinners. One such factor is OSA, which shares many of the same risk factors as PE, including advanced age, physical inactivity, and obesity.

"There is growing evidence from cross-sectional and longitudinal studies that <u>obstructive sleep apnea</u> is a risk factor for <u>pulmonary embolism</u>," explained lead investigator Alberto Alonso-Fernández, MD, PhD, Hospital Universitario Son Espases, Palma de Mallorca, Spain. "This association represents a major public health burden, given the high prevalence of both disorders and the mortality rates of PE. However, to our knowledge, no <u>longitudinal studies</u> to date have explored the role of



OSA as a risk factor for recurrent thromboembolic events."

The study followed 120 patients for five to eight years after their first occurrence of PE. During the study, their sleep was monitored for signs of OSA. Investigators found that 19 of the patients had recurrent PE during the follow-up period and of those 19 patients, 16 of them suffered from OSA.

"The main finding in this study is that after a first episode of PE, patients with OSA had a higher risk of recurrent PE than those without OSA," said Dr. Alonso-Fernández. "Moreover, AHI and nocturnal hypoxemia, assessed by the mean nocturnal oxygen saturation and percentage of total time the patient spent with their oxygen saturation below 90%, are independent risk factors for PE recurrence and for resuming anticoagulation because of a new thromboembolic event."

Addressing why OSA may make people more susceptible to subsequent PE events, Dr. Alonso-Fernández stated, "PE is the result of Virchow's classic risk triad, namely vascular endothelial impairment, stasis of blood flow, and/or increased coagulability. OSA could hypothetically affect all three mechanistic pathways. Intermittent hypoxia increases oxidative stress, and inflammatory response that impairs endothelial function. OSA-related hemodynamic alterations and sedentarism may slow intravenous flow, and lastly, increased coagulability, platelet activity, and decreased fibrinolytic capacity in OSA may be improved after CPAP."

While much attention has been paid to what causes the first PE, only a few known influencers have been identified as playing a role in recurrent PE, including cancer, continued estrogen use, vena cava filters, high post-anticoagulation D-dimer, male gender, and obesity. The current study found OSA is an independent risk factor for recurrent PE, even after adjusting for several factors including BMI. OSA is a common problem among obese people and investigators assert that the risk of recurrent PE



that is attributed to obesity might be partially related to OSA.

"Obesity is associated with sedentarism and venous stasis, and it has also been related to impaired fibrinolysis and high concentrations of clotting factors that might lead to a prothombotic state that can further increase because obesity is associated with high estrogen levels and chronic low-grate inflammation," proposed Dr. Alonso-Fernández. "It is tempting to speculate that OSA and obesity may additively or synergistically lead to up-regulation of procoagulant activity that may intensify the risk of PE recurrence."

Knowing that OSA is an <u>independent risk factor</u> for recurrent PE is important information that can help physicians better understand treatment options. CPAP use is a proven intervention for OSA and patients with OSA may need to stay on anticoagulation therapy longer to reduce their risk for another PE. "Given the high prevalence of OSA in patients with PE, the procoagulability state induced by the intermittent hypoxia, and the risk for PE recurrence, the potential of CPAP and/or extend oral anticoagulation to reduce PE recurrence and mortality in patients with PE and OSA clearly warrants further study," concluded Dr. Alonso-Fernández.

More information: Alberto Alonso-Fernández et al, OSA Is a Risk Factor for Recurrent VTE, *Chest* (2016). DOI: 10.1016/j.chest.2016.07.011

Provided by Elsevier

Citation: Sleep apnea can contribute to recurring pulmonary embolism (2016, December 7) retrieved 2 May 2024 from

https://medicalxpress.com/news/2016-12-apnea-contribute-recurring-pulmonary-embolism.html



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