

**Meta-analysis of comorbidity between cerebrovascular disease (CVA) and periodic limb movements in sleep (PLMS)**

Ping-Tao Tseng <sup>a</sup>, Yen-Wen Chen <sup>b</sup>, Pao-Yen Lin <sup>c,d</sup>, Meng-Ni Wu <sup>e</sup>, Chung-Yao Hsu <sup>f,g</sup>

<sup>a</sup> Department of Psychiatry, Tsyrr-Huey Mental Hospital, Kaohsiung Jen-Ai's Home, Taiwan

<sup>b</sup> Prospect clinic for otorhinolaryngology & neurology

<sup>c</sup> Department of Psychiatry, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan

<sup>d</sup> Center for Translational Research in Biomedical Sciences, Kaohsiung Chang Gung Memorial Hospital

<sup>e</sup> Department of Neurology, Kaohsiung Medical University Hospital

<sup>f</sup> Department of Neurology, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

<sup>g</sup> Department of Neurology, Faculty of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

## **Abstract:**

### **Introduction**

Periodic limb movement in sleep (PLMS) has been shown to increase the autonomic hyperactivities and increase the risk of vascular disease. Some researches had provided evidence of potential association between PLMS and cerebrovascular disease (CVA). However, this is inconclusive based on current evidences. Therefore, we conducted a systematic review and meta-analysis to summarized the current evidence of association between the PLMS and the CVA.

### **Method and Materials**

Two independent authors performed data search on the electronic platform PubMed, ScienceDirect, and ClinicalTrials.gov with inclusion criteria of “(1) published articles investigating the comorbidity between PLMS and CVA, either in forms of ischemic stroke or hemorrhagic stroke, and (2) articles that were observed clinical trials in humans” and hand search for other potential eligible articles from the reference list of review articles. The exclusion criteria were (1) animal studies, and (2) trials conducted for the comorbidity other than PLMS and CVA. The primary outcome measure was the prevalence rate of (i) CVA, either in forms of ischemic stroke or hemorrhagic stroke in patients with PLMS or without PLMS, or (ii) the difference of PLM index in patients with CVA or without CVA. The PLM index was defined as PLM happened at sleep (PLM/hour), which was recorded by polysomnography. Meta-regression and subgroup meta-analysis were done for potential heterogeneity.

### **Result**

After excluding thirty-nine articles, six articles were recruited in current meta-analysis and release 179 patients with CVA (mean age=63.5, mean female proportion=32.9%) versus 122 controls without CVA (mean age=63.5, mean female proportion=30.9%). On the other hand, there were 2125 patients with PLMS (mean age=76.3, mean female proportion=0.6%) and 1048 controls without PLMS (mean age=71.4, mean female proportion=8.2%).

The main results of meta-analysis of difference of PLM index in patients with CVA and controls without CVA showed significantly higher PLM index in patients with CVA than those in controls without CVA (Hedges'  $G = 0.860$ , 95% CI = 0.359 to 1.361,  $P = 0.001$ ) with significant heterogeneity (Q value = 14.80,  $df = 3$ ,  $P = 0.002$ ;  $I^2 = 79.73\%$ ) but no publication bias via Egger's regression (t value = 0.29,  $df = 2$ ,  $p = 0.802$ ). In contrary, the meta-analysis of prevalence rate of CVA in patients with/without PLMS revealed that there was no any significantly different comorbidity rates of CVA in patients with PLMS and those in controls without PLMS (Odds ratio = 1.202, 95% CI = 0.897 to 1.609,  $P = 0.218$ ).

## **Conclusion**

Current meta-analysis could only provide evidence about the higher PLM index in patients with CVA than those without CVA but not the evidence about the prevalence of CVA in patients with PLMS. We encourage further study to clarify the potential association between these two diseases.