Relationship Between Zolpidem Use and Aortic Dissection Risk: A Taiwanese Population–Based Case-Control Study

Yen-Nien Lin, M.D. 1,2; Chih-Ping Chang, M.D. 1,2; Chen-Chia Yang, M.D. 1,2; Chiung-Ray Lu, M.D. 1,2; Fung-Chang Sung, 3,4 Shih-Ni Chang, 3,4 and Jen-Jyh Lin, M.D. 1,2; Po-Yen Ko, M.D. 1,2

1. Division of Cardiology, Department of Medicine, China Medical University Hospital, Taichung 40447, Taiwan
2. China Medical University, Taichung 40402, Taiwan
3. Management Office for Health Data, China Medical University Hospital, Taichung, Taiwan
4. Institute of Environmental Health, College of Public Health, China Medical University, Taichung, Taiwan

Address correspondence to:
Po-Yen Ko, M.D.
Division of Cardiology, Department of Medicine, China Medical University Hospital
2 Yuh-Der Road, Taichung, 40447, TAIWAN
Tel: 886-4-22052121, Ext.: 2371
Fax: 886-4-23602467
E-Mail: kpy0907@gmail.com

**Running title:** Zolpidem and Aortic dissection

**Key words:** zolpidem, aortic dissection, insomnia

**Footnote:** Yen-Nien Lin and Chih-Ping Chang contributed equally to the work. This study will be presented in part at the American Heart Association’s Resuscitation Science Symposium 2013 in Dallas, Texas.

**Acknowledgments:**

This study was partly supported by grants from the Taiwan Department of Health Clinical Trial and Research Center for Excellence (DOH102-TD-B-111-004), and Taiwan Department of Health Cancer Research Center for Excellence (DOH102-TD-C-111-005)
ABSTRACT

Objective: To evaluate the relationship between the use of zolpidem and risk of subsequent aortic dissection in Taiwanese patients.

Method: This case-control study used data obtained from the National Health Insurance Research Database to determine whether the use of zolpidem is associated with an increased risk of aortic dissection. The case group comprised 1314 patients who were newly diagnosed with aortic dissection between January 1, 2003, and December 31, 2010. We also randomly selected a 4-fold greater number of patients without aortic dissection as a control group. Patients were frequency-matched with controls on sex, age, and year of index date. We measured the effect of zolpidem, and determined the adjusted odds ratios (ORs) with 95% confidence intervals (CIs).

Results: We found that exposure to zolpidem was associated with increased risk of aortic dissection (OR=1.59; 95% CI, 1.36–1.86). The risk of aortic dissection increased significantly with increasing exposure to zolpidem; for average exposures of ≤40, 41-160, 161-690, and >690 mg/year, the ORs were 1.45, 1.36, 2.08 and 1.55, respectively; the P value for the trend was <0.001. Regardless of whether people presented with a sleep disorder, the risk of aortic dissection increased with zolpidem exposure; the adjusted OR was 1.70 without sleep disorder and 1.62 with sleep disorder.
**Conclusions:** This population-based study positively associated the use of zolpidem with increased risk of Aortic dissection. Our findings warrant further large-scale and in-depth investigations in this area.