**Supplementary Table 1.** Characteristics of the study population aged 40 or older and diagnosed with angina in Korea; 2014a

|  |  |  |  |
| --- | --- | --- | --- |
| Characteristics | Total, n (%)(n= 1,263,616) | TMZ group, n (%)(n= 72,299) | No-TMZ group, n (%)(n= 1,191,317) |
| Sex |  |  |  |  |  |  |
| Male | 654,191 | 51.8 | 33,300 | 46.1 | 620,891 | 52.1 |
| Female | 609,426 | 48.2 | 39,000 | 53.9 | 570,426 | 47.9 |
| Age (years) |  |  |  |  |  |  |
| 40-64 | 596,627  | 47.2  | 31,533 | 43.6 | 565,094 | 47.4 |
| ≥65 | 666,989  | 52.8  | 40,766 | 56.4 | 626,223 | 52.6 |
| Insurance type |  |  |  |  |  |  |
| Health insurance | 1,162,951  | 92.0  | 66,299  | 91.7  | 1,096,652  | 92.0  |
| Medical aid  | 100,665  | 8.0  | 6,000  | 8.3  | 94,665  | 8.0  |
| Concurrent medicationsb |  |  |  |  |  |  |
| Typical antipsychotics | 26,800  | 2.1  | 2,100  | 2.9  | 24,700  | 2.1  |
| Atypical antipsychotics | 39,233  | 3.1  | 2,033  | 2.8  | 37,200  | 3.1  |
| Calcium-channel blocker (Flunarizine)  | 34,200  | 2.7  | 5,000  | 6.9  | 29,200  | 2.5  |
| Antiemetics | 476,994  | 37.8  | 33,433  | 46.2  | 443,561  | 37.2  |
| Comorbidity |  |  |  |  |  |  |
| Diabetes | 611,291  | 48.4  | 34,566  | 47.8  | 576,725  | 48.4  |
| Stroke | 190,664  | 15.1  | 12,367  | 17.1  | 178,297  | 15.0  |
| End-stage renal disease | 20,533  | 1.6  | 1,033  | 1.4  | 19,500  | 1.6  |
| Alzheimer’s disease | 8,600  | 0.7  | 767  | 1.1  | 7,833  | 0.7  |
| Outcome |  |  |  |  |  |  |
| Parkinsonism | 25,433  | 2.0  | 2,100  | 2.9  | 23,333  | 2.0  |

aWeighted for all variables in the table based on 37,909 patients.

bConcurrent medications reported as drugs known to induce parkinsonism.

Abbreviation: TMZ, trimetazidine.

**Data Supplementary**

For the primary analysis, we used the full logistic regression model containing all independent variables: sex (male, female), age (40-64, ≥65), insurance type (health insurance, medical aid), drug classes (typical antipsychotics, atypical antipsychotics, flunarizine, antiemetics) and cormorbidities (diabetes, stroke, end-stage renal disease and Alzheimer’s disease). Confounders were identified based on previous articles related to drug-induced parkinsonism [1-5]. We then performed a forward stepwise logistic regression analysis (α for entry and retention; 0.05 and 0.10 respectively) including all of independent variables and calculate the adjusted OR from the final model which included sex, age, insurance type, typical antipsychotics, atypical antipsychotics, flunarizine, stroke and Alzheimer’s disease as confounders. We tested for the interaction terms between TMZ and each of the confounders, and no significant interactions were observed between TMZ and each of the confounders. Discrimination was evaluated using the c-statistics [6] and calibration was assessed by the Hosmer–Lemeshow test [7]. The c-statistics of the full model and the stepwise model were 0.661 (95% CI 0.641-0.682) and 0.659 (95% CI 0.639-0.679) respectively, which indicate weak predictive models. As the HIRA claims data does not provide detailed information such as obesity, smoking status, physical activity level, environmental factors or genetic factors, all of which were possible confounders, the models could not have a good discrimination. The models were well-calibrated with a Hosmer–Lemeshow goodness of fit test statistics of 4.29 (full, p=0.746) and 1.49 (stepwise, p = 0.914). We performed subgroup analysis using the same method as above. We then performed a forward stepwise logistic regression analysis (α for entry and retention; 0.05 and 0.10 respectively) including all of independent variables and calculate the adjusted OR from the final model which included age and stroke as confounders. The c-statistics of the full model and the stepwise model were 0.689 (95% CI 0.617-0.761) and 0.662 (95% CI 0.593-0.731) respectively. The models were well-calibrated with a Hosmer–Lemeshow goodness of fit test statistics of 4.87 (full, p=0.771) and 0.88 (stepwise, p = 0.645).

1 Huang HC, Tsai CH, Muo CH, Lin KH, Lu MK, Sung FC, Kao CH: Risk of Parkinson's disease following zolpidem use: a retrospective, population-based cohort study. J Clin Psychiatry 2015;76:e104-110.

2 Wang IK, Lin CL, Wu YY, Chou CY, Lin SY, Liu JH, Yen TH, Huang CC, Sung FC: Increased risk of Parkinson's disease in patients with end-stage renal disease: a retrospective cohort study. Neuroepidemiology 2014;42:204-210.

3 Lin HL, Lin HC, Tseng YF, Chen SC, Hsu CY: Risk of parkinsonism induced by flunarizine or cinnarizine: a population-based study. Eur J Clin Pharmacol 2017;73:365-371.

4 Korczyn AD: Vascular parkinsonism—characteristics, pathogenesis and treatment. Nature reviews neurology 2015;11:319.

5 Ma H-I, Kim J-H, Chu M-K, Oh M-S, Yu K-H, Kim J, Hahm W, Kim YJ, Lee B-C: Diabetes mellitus and drug-induced parkinsonism: A case–control study. Journal of the neurological sciences 2009;284:140-143.

6 Steyerberg EW: Clinical Prediction Models: A Practical Approach to Development, Validation and Updating. New York, Springer, 2009; 260-263.

7 Hosmer DW, Lemeshow S: Applied Logistic Regression. Second Edition. New York, Wiley, 2000.