

# 台灣腦中風學會摘要用紙

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第十屆第一次會員大會暨一〇一〇年度學術研討會 請用鉛筆打勾  口頭  壁報

## 慢性阻塞性肺病合併使用長效性抗膽鹼製劑及長效型乙型致效劑之中風發生率之探討—以台灣健保資料庫分析之回溯性世代研究

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The incidence of stroke in combination of long-acting anticholinergic agents and long-acting  $\beta_2$ -adrenergic receptor agonist in patients with COPD: a retrospective cohort study using Taiwan National Health insurance database

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**Background and Purpose:** Accumulated evidence showed combination of long-acting anticholinergic agents (LAAC) and long-acting  $\beta_2$ -adrenergic receptor agonist (LABA) has efficacy in improving lung function test and quality of life compared with monotherapy in patient with COPD, especially in patients with severe COPD. However, recent large retrospective studies showed long-acting anticholinergic agents increased the incidence of stroke and cardiac events. Whether combination of LAAC and LABA increased the incidence of stroke or other cardiac events were still unclear. The purpose of this study is to compare the incidence of stroke and other cardiovascular diseases in combination with long-acting anticholinergic agents and long-acting  $\beta_2$ -adrenergic receptor agonist with single agent use ( long-acting anticholinergic agents or long-acting  $\beta_2$ -adrenergic receptor agonist) in patients with COPD using Taiwan National Health insurance database.

**Methods:** A cohort of patients diagnosed as COPD between 1997 and 2008 using longitudinal national health insurance research database [LHID], 2005 in Taiwan. The patients who has pre-existed stroke or cardiovascular diseases were excluded from studies. From 994,857 subjects diagnosed as COPD, 596 subjects who used at least one of long-acting anticholinergic agents (LAAC) or long-acting  $\beta_2$ -adrenergic receptor agonist (LABA) continuously for at least one year and had no pre-existed stroke or cardiovascular diseases at the time of inclusion were selected by pre-defined criteria. Among them, 196 subjects used long-acting anticholinergic agents, 318 subjects used long-acting  $\beta_2$ -adrenergic receptor agonist and 82 subjects used combination of these two agents. The adjusted factor included age, sex, comorbidity and steroid use. SAS 9.3 was used to conduct statistic analyses. Univariate regression analysis was performed to calculate the hazard ratio and 95% confidence interval and log rank test was use to analyze survival curve between groups.

**Results:** There were no significant difference in age, sex, comorbidity (DM, hypertension,

hyperlipidemia) and steroid use between three groups (LAAC, LABA and combination of LAAC and LABA). There were no significant difference in the incidence of cardiac failure ( $p=0.8446$ ), arrhythmia ( $p=0.7803$ ), myocardial infarction ( $p=0.7405$ ) and angina ( $p=0.7296$ ) between three groups, whereas, there were significant difference in the incidence of stroke ( $p=0.0033$ ) between three groups. The incidence of stroke in LAAC, LABA and combination of LAAC and LABA were 2.04%, 1.26% and 8.53%, respectively. Furthermore, there were significant difference in onset time of stroke between three groups ( $p<0.0001$ ). The onset time of stroke in LAAC, LABA and combination of LAAC and LABA were  $898.39\pm 9.60$ ,  $1495.20\pm 9.06$  and  $1147.52\pm 49.26$  days, respectively. Survival analysis showed significant decrement of survival rate in combination of LAAC and LABA ( $P=0.0001$ ). Co-medication of LAAC and LABA had significant higher hazard ratio 1.03 (95% CI: 1.01-2.93) related to single use of LABA and 2.98 (95% CI: 0.73-3.35) related to single use of LAAC in the incidence of stroke.

**Conclusion:** this cohort study using Taiwan National Health insurance database showed combination of LAAC and LABA in patients with COPD may be associated with the increase of incidence of stroke compared with either agent alone. We should be especially cautious about the co-medication of LAAC and LABA in patients with COPD.

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