**Real-world evidence on the risk of acute cardiovascular events among elderly hypertensive patients treated with calcium channel blockers in secondary cardiovascular prevention**

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**Introduction:** Different studies correlated calcium channel blockers (CCBs), and in particular short-acting formulations, with increased risks of acute cardiovascular (CV) events and mortality. Nevertheless, antihypertensive treatment with CCBs is still routinely used in clinical practice, both in primary and secondary CV prevention. This study aimed therefore to provide real-world evidence from the Italian clinical practice on the risk of acute CV events related to the different CCBs classes among CV-compromised hypertensive elderly. This study is part of an Italian project funded by the Italian Medicines Agency.

**Methods:** A nested user-only case-control study was performed on the administrative databases of 3 Italian Regions and 2 Local Health Authorities. A cohort of 107,533 CCB users aged ≥ 65 years who were discharged for CV outcomes in the years 2008-2010 was followed until 2011-2014. The 27,679 patients who experienced hospital admission for further CV events during follow-up were included as cases. To each case, up to 4 controls were matched by gender, age, geographical unit, and date of first CV-related hospitalization. Current use of the different CCBs classes (short-acting dihydropyridines (DHPs); long-acting DHPs; short-acting non dihyopyridinic CCBs (n-DHPs); and long-acting n-DHPs) was compared among cases and controls. The risk of acute CV events associated with current use of the different CCBs classes was modelled by fitting conditional logistic regression. To minimize the risk of misclassifying exposition due to therapies administered within hospital stays, a sensitivity analysis was performed, excluding all patients who experienced an all-cause hospitalization in the 30 days before the index date (i.e. date of the acute CV event for cases; matched date for controls).

**Results:** 55,325 controls were matched to 25,204 case subjects. The majority of subjects were women, and were aged between 70 and 84. Compared with past users, current users of CCBs exhibited a risk reduction of 12% (OR 0.88 [95% CI: 0.84-0.91]) for acute CV events.

In particular, current users of long-acting DHPs were at the lowest risk (OR 0.87 [0.84 – 0.90]). On the other hand, current use of short-acting CCBs was associated with a significant increase in risk (OR 1.77 [1.13– 2.78] for short-acting DHPs; 1.19 [1.07 – 1.31] for short-acting n-DHPs).

The sensitivity analysis performed on 11,672 cases and 8,427 controls further confirmed these results.

**Conclusion:** Evidence that current use of short-acting CCBs is associated to a higher risk of acute CV events among hypertensive elderly with CV diseases was consistently supplied by this wide-population study. According to our findings, long-acting CCBs formulations should be preferred, especially in elderly CV-compromised subjects.