

中文題目：使用噻嗪類利尿劑於慢性腎臟病病人與臨床預後相關性研究：一個全國性世代研究

英文題目：Association of Thiazide Diuretics Usage and Clinical Outcomes in Chronic Kidney Disease: Analysis of the Nationwide Cohort Study

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Background: CKD (chronic kidney disease) is associated with sodium retention, which causes edema syndrome and hypertension. Patients with uncontrolled hypertension has a higher risk of cardiovascular events as well as end-stage renal disease (ESRD) and mortality. Thiazides (THZ) are used widely for the treatment of both volume overload and hypertension. Beyond diuretic effect, THZ can activate the calcium-activated potassium (BK) channel in vascular smooth muscles, resulting in vasorelaxation. There are limited data investigating THZ effects in the cardiovascular (CV) and non-cardiovascular outcomes. The aim of this study is to examine the clinical effects of THZ usage in patients with CKD by utilizing a nationwide cohort.

Methods: This longitudinal nationwide population-based cohort study investigated the prognosis in 17,002 CKD patient. The THZ cohort included 8501 patients; each patient was age- and sex-matched with one THZ nonuser in the CKD population. The Cox proportional hazard regression analysis was conducted to estimate the effects of THZ on the mortality, incidence of ESRD, congestive heart failure (CHF), acute myocardial infarction (AMI), peripheral arterial occlusive disease (PAOD) and stroke.

Results: The mortality rate was significantly lower in THZ users than in THZ nonusers (hazard ratio [HR] = 0.65; 95% confidence interval [CI] = 0.60 - 0.71, $p < 0.001$). The HR for the incidences of ESRD, AMI, PAOD and stroke were significantly ($p < 0.05$) lower in THZ users (HR=0.71, CI= 0.66 - 0.77; HR=0.82, CI=0.76-0.89; HR=0.68, CI=0.63-0.74; HR=0.91, CI=0.84-0.98) than in THZ nonusers. In THZ subgroup analysis, Chlorthalidone users had significantly lower incidences of mortality, ESRD, and PAOD (HR=0.62, CI= 0.40 - 0.97, $p = 0.037$; HR=0.54, CI=0.36-0.82, $p = 0.004$; HR=0.60, CI=0.39-0.94, $p = 0.026$) than nonusers.

Indapamide users had significant lower incidences of mortality, ESRD, AMI and PAOD (HR=0.64, CI= 0.57 – 0.71, $p<0.001$; HR=0.72, CI=0.65-0.79, $p<0.001$; HR=0.89, CI=0.81-0.98, $p=0.018$; HR=0.69, CI=0.62-0.78, $p<0.001$) than nonusers.

Further, in the THZ subtype analysis, Metolazone users had significantly higher incidences of ESRD, CHF, and AMI (HR=1.28, CI= 1.06 – 1.54, $p=0.009$; HR=1.60, CI=1.33-1.92, $p<0.001$; HR=1.41, CI=1.08-1.59, $p=0.007$) than nonusers. Both Chlorthalidone and Indapamide had better outcome (HR; 95% confidence interval [CI] = 0.35-1.2).

Conclusion: In patients with CKD who receive therapy with THZ, both Chlorthalidone and Indapamide users exhibited significantly beneficial effects of mortality, ESRD, and PAOD. Indapamide users revealed significantly advantageous results of AMI. However, Metolazone users had significantly higher incidences of ESRD, CHF, and AMI. A further randomized control trial to clarify the effect of THZ usage in patients with CKD is a necessity.

Key words: chronic kidney disease, nationwide population-based cohort study, thiazides

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