Effects of Thiazide-Type and Thiazide-Like Diuretics on Cardiovascular Events and Mortality
Systematic Review and Meta-Analysis

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Abstract—Thiazide diuretics are recommended as first-line therapy for hypertension and are among the most commonly prescribed drugs worldwide. According to their molecular structure, thiazide diuretics can be divided in thiazide-type (TT) and thiazide-like (TL) diuretics. TL diuretics have a longer elimination half-life compared with TT diuretics and have been shown to exert additional pharmacological effects, which may differently affect cardiovascular risk. In this meta-analysis, we compared the effects of TT and TL diuretics on cardiovascular events and mortality. Randomized, controlled studies in adult hypertensive patients that compared TT or TL diuretics with placebo or antihypertensive drugs and had ≥1 year follow-up were included. Primary outcome was cardiovascular events; secondary outcomes included coronary events, heart failure, cerebrovascular events, and all-cause mortality. Meta-regression analysis was used to identify confounders and correct for the achieved blood pressure reductions. Twenty-one studies with >480 000 patient-years were included. Outcomes were not affected by heterogeneity in age, sex, and ethnicity among included studies, whereas larger blood pressure reductions were significantly associated with increased risk reductions for all outcomes (P<0.001). Corrected for differences in office blood pressure reductions among trials, TL diuretics resulted in a 12% additional risk reduction for cardiovascular events (P=0.049) and a 21% additional risk reduction for heart failure (P=0.023) when compared with TT diuretics. The incidence of adverse events was comparable among TT, TL diuretics, and other antihypertensive therapy. Our data suggest that the best available evidence seems to favor TL diuretics as the drug of choice when thiazide treatment is considered for hypertension. (Hypertension. 2015;65:00-00. DOI: 10.1161/HYPERTENSIONAHA.114.05122.)

Key Words: blood pressure ■ cardiovascular diseases ■ diuretics ■ heart failure ■ hypertension ■ thiazides

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DOI: 10.1161/HYPERTENSIONAHA.114.05122