

# Safety and Efficacy of Anti-Hypertensive Medications in Patients with Heart Failure with Preserved Ejection Fraction: A Systematic Review and Meta-analysis

Mohammad Alqadi, MD<sup>1\*</sup>

<sup>1</sup>Division of Internal Medicine, Department of Medicine, The University of Toledo, Toledo, OH 43614

\*Corresponding author: [mohammad.alqadi@utoledo.edu](mailto:mohammad.alqadi@utoledo.edu)

**Key Words:** HFpEF, Hypertension, Antihypertensive agents, Outcomes

Published: 14 December 2023

**Introduction:** Hypertension (HTN) is a co-morbidity that is commonly associated with heart failure (HF) with preserved ejection fraction (HFpEF). This meta-analysis aims to evaluate the association of anti-hypertensive medications (AHM) therapy with cardiovascular (CV) outcomes in patients with HFpEF.

**Objectives:** Treatment of HTN in HFpEF patients is associated with improved CV outcomes.

**Methods:** Performed a database search (OVID Medline, Web of Science, and Embase) for studies reporting the association of AHM with CV outcomes in patients with HFpEF. The primary endpoint was all-cause mortality. Secondary endpoints include CV mortality, worsening HF, CV hospitalization, and major adverse CV events (MACE).

**Results:** A total of 15 studies with 17507 HFpEF participants (8732 treated with medical therapy vs 8775 treated with placebo) met inclusion criteria. Use of AHM was not associated with lower all-cause mortality or CV mortality compared to treatment with placebo (OR 1.01, 95% CI 0.80-1.27;  $p=0.95$ , OR 0.97, 95% CI 0.86-1.08;  $p=0.53$ ). Use of AHM was associated with a statistically significant lower risk of MACE and CV hospitalization (OR 0.90, 95% CI 0.83-0.97;  $p<0.01$ , OR 0.89, 95% CI 0.81-0.97;  $p<0.04$ ). Subgroup analysis demonstrated this to be primarily driven by studies with mixed HFpEF patients with or without HTN, not HFpEF patients with HTN. There was a non-significant trend toward lower risk of worsening HF in patients treated with AHM, and was driven by HFpEF patients with or without HTN, not HFpEF patients with HTN (OR 0.87, 95% CI 0.78-0.97;  $p=0.02$  versus OR 0.57, 95% CI 0.18-1.86;  $p=0.35$ ).

**Conclusion:** While treatment with anti-hypertensives was not associated with lower risk of all-cause mortality, their use may be associated with reduced risk of adverse CV outcomes in patients with HFpEF regardless of whether they have HTN. Further studies are needed to clarify this association and determine the effect based classes of medications.