HIGH VERSUS LOW DOSE ACE INHIBITORS IN HEART FAILURE PATIENTS

**Introduction:** Angiotensin converting-enzyme inhibitors (ACEIs) have shown to reduce mortality and hospitalization and are the first-line treatment in heart failure (HF). Even though guidelines recommend to up-titrate ACEIs to target doses, the beneficial is uncertain and low doses may promote similar outcomes. We aim to systematically review evidence comparing the effect of low and high-dose angiotensin converting-enzyme inhibitors (ACEIs) in HF on all-cause mortality and hospitalization.

**Methods:** We searched PubMed, Embase, Cochrane CENTRAL and LILACS up to June 2018. We included randomized clinical trials (RCTs) comparing low and high-dose ACEIs in adults with HF with reduced left ventricular ejection fraction (HFrEF). Study selection and data extraction were performed by two independent reviewers. Risk of bias was assessed with RoB 2.0 and quality of evidence with Grading of Recommendations Assessment, Development and Evaluation (GRADE). We conducted random-effects meta-analysis. PROSPERO registration: CRD42017070397

**Results:** We included 8 RCTs (5829 HF patients). In comparison with low dose ACEIs, high dose ACEIs showed non-significant effects on all-cause mortality (8 RCTs, n=5828, RR 0.95 [95%CI 0.88 - 1.02], moderate quality of evidence), and all-cause hospitalization (5 RCTs, n=5394, RR 0.95 [95%CI 0.82 - 1.10], moderate quality of evidence).

**Conclusions:** Our results suggest that the magnitude of benefit of using high-dose versus low- to intermediate dose ACEi might be less that traditionally attributed in clinical guidelines. These findings might help clinicians to address the complex task of HF management in a more rational and timely fashion, saving efforts to implement strategies with the greatest net clinical benefit.

**KEY-WORDS:** Angiotensin converting-enzyme inhibitor; high dose; low dose; heart failure; systematic review.