EARLY AND LATE EFFECTS OF ANGIOTENSIN RECEPTOR BLOCKADE ON KIDNEY FUNCTION IN PATIENTS WITH CHRONIC HEART FAILURE

ACC Moderated Poster Contributions
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Background: The effect of high versus low-dose angiotensin-receptor blocker (ARB) on kidney function, its time course, and its relation to longer-term outcomes in patients (pts) with heart failure (HF) are unknown.

Methods: HEAAL randomized 3,834 HF pts to 150 or 50 mg losartan daily. Early Worsening Kidney Function (WKF) was defined as glomerular filtration rate (GFR) reduction >25% prior to 4 months, and Late WKF as WKF after 4 months. Using mixed model analyses, GFR slopes were estimated up to and beyond 4 months of treatment. Proportional hazard models were used to evaluate the relationship of WKF to clinical outcomes with a median patient follow up of 4.7 years.

Results: Compared to 50 mg, losartan 150 mg caused greater GFR reduction (p<0.0001) (Figure 1a). With losartan 150mg, GFR declined through 4 months (-.424 ml/min/1.73m2/month (-0.633, -0.214)). After 4 months, decline in GFR slowed (-0.087 (-0.099, -0.075); p<.0001) (Figure 1b). Similar trends were seen in the 50 mg group, with minimal late between-group difference. Early WKF in the total population had a smaller impact on mortality and HF-hospitalization than Late WKF (HR=1.31 [95% CI (1.3, 1.51)] vs. HR= 1.70 [95% CI (1.49, 1.94)] (p=.002).

Conclusions: Compared to low-dose, high-dose losartan leads to greater early GFR reduction, but with little difference in later rates of change. Early (likely hemodynamic) change in GFR following ARB initiation has less implication for adverse outcomes than late effects.