

## Blocking RAAS Cascade in Chronic Heart Failure Therapy: from Renin Inhibitor, ACE Inhibitor, Angiotensin Receptor Blocker to Aldosterone Receptor Blocker

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The prevalence of chronic heart failure (CHF) is increasing due to increased aged population. CHF leads to frequent hospitalization and causes health burden. CHF is characterized by a vicious cycle in which the progression in myocardial dysfunction stimulates a compensatory neurohumoral activation that perpetuates left ventricular hypertrophy and dilatation. The goal of therapy for CHF is to reduce mortality and morbidity, to prevent further myocardial damage and increase quality of life.

Renin-angiotensin-aldosterone system (RAAS) is activated in CHF and plays a major pathophysiological role in CHF. Inhibitors for RAAS have been developed to lower blood pressure and treat CHF. Inhibitors of RAAS include ACE inhibitor, ARB blocker, aldosterone receptor antagonist and rennin inhibitor. ACE inhibitor is the first one to show the beneficial effect in the management of CHF. Landmark clinical trials and meta-analysis have demonstrated the beneficial effect of ACE inhibitors in reducing mortality and hospitalization in patients with CHF. An ACE inhibitor is recommended in all patients with heart failure with LVEF<40%. In hospitalized patients with heart failure, ACE inhibitors should be initiated before discharge.

Treatment with an ARB improves LV function, patient well-being and reduces hospital admission for worsening heart failure. An ARB is recommended in all patients with heart failure and LVEF<40% who remain symptomatic despite optimal therapy with an ACE inhibitor and beta-blocker. ARB can be an alternative therapy in patients intolerant of an ACE inhibitor. Aldosterone antagonists reduce hospital admission for worsening heart failure and increase survival when added to existing therapy including an ACE inhibitor. The addition of aldosterone antagonist is recommended in all patients with LVEF<35%, severe symptomatic heart failure without hyperkalemia or significant renal dysfunction. Routine combined use of an ACE inhibitor, ARB and aldosterone antagonist is not recommended for patients with current or prior symptoms of heart failure and reduced LVEF.

The role of renin inhibitor in treatment of CHF has not been established. In ASPIRE trial, rennin inhibitor with aliskiren did not significantly improve LV function in post-myocardial infarction patients under standard medical therapy as compared to placebo. The adverse events increased in patients treated with aliskiren.