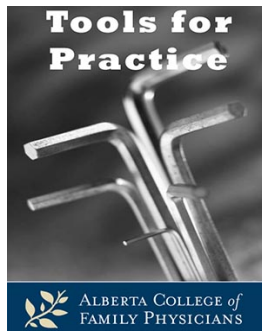


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Aldosterone antagonists in systolic heart failure – no longer an afterthought.

Clinical Question: What is the role of aldosterone antagonists in patients with chronic systolic heart failure?

Bottom-line: Aldosterone antagonists reduce mortality and hospitalizations in patients with congestive heart failure (Class II–IV). The benefit appears similar to β -blockers or ACE inhibitors. Close monitoring is required for those at risk of hyperkalemia.

Evidence:

- Two randomized controlled trials:
 - RALES:¹ 1,663 patients with Class III–IV heart failure on ACE inhibitors and diuretics. Given spironolactone or placebo. At 24 months:
 - Statistically significant reduction in:
 - Mortality: spironolactone 35%, placebo 46%, Number Needed to Treat (NNT) 10.
 - Cardiovascular hospitalization: 32% vs. 40%, NNT 12.
 - Adverse events:
 - Gynecomastia/breast pain: spironolactone 10%, placebo 1%, Number Needed to Harm (NNH) 11.
 - Serious hyperkalemia (potassium ≥ 6 mmol/L): not statistically different.
 - EMPHASIS-HF:² 2,737 patients with Class II heart failure with majority on ACE inhibitors, and β -blockers. Given eplerenone or placebo. At 21 months:
 - Statistically significant reduction in:
 - Mortality: eplerenone 13%, placebo 16%, NNT 34.
 - Cardiovascular hospitalization: 22% vs. 29%, NNT 15.
 - Adverse events:
 - Hyperkalemia (>5.5 mmol/L) increased with eplerenone 12%, placebo 7%, NNH 22.
 - No difference in gynecomastia or renal failure.
- Two meta-analyses found similar results.^{3,4}

Context:

- Aldosterone antagonists compare favourably to other agents used in congestive heart failure whose relative risk reductions for mortality are:
 - Aldosterone antagonists^{1,2} ~25%.
 - β -blockers⁵ ~29%.
 - ACE inhibitors^{6,7} ~23%.
- Aldosterone antagonists are prescribed at less than half the rate of β -blockers and ACE inhibitors, and represent the greatest potential for increased systolic heart failure survival.⁸
- Titration to target doses of ACE inhibitors and β -blockers before adding aldosterone antagonists has been advocated,⁹ however the rates/doses of these medications were quite different in RALES and EMPHASIS-HF, yet they had similar outcomes.
- There is no head-to-head trial of spironolactone vs. eplerenone. Spironolactone (\$12/month) could be used first and, if gynecomastia/breast pain develop, switch to eplerenone (\$100/month).

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