Hyperkalemia in Heart Failure

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Potassium “Problems” and HF

Hypokalemia and Hyperkalemia are common in HF patients.

Diuretics cause increases in urinary K+ excretion resulting in hypokalemia.

While RAS blockers, especially AA such as spironolactone can result in hyperkalemia.

Hyperkalemia can be so significant that EB therapies need to be reduced or stopped.
Hypokalaemia and ventricular fibrillation in acute myocardial infarction

J E NORDREHAUG, G VON DER LIPPE

From the Department of Medicine, Diakonissehjemmets Sykehus, Haraldsplass, Bergen, Norway
# Extensive Use of Guideline-Recommended Therapies at Baseline

<table>
<thead>
<tr>
<th>Therapies and Treatments at Randomization, % (n)</th>
<th>Sacubritil/Valsartan (n=4187)</th>
<th>Enalapril (n=4212)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prettrial use of ACE inhibitor*</td>
<td>78.0 (3266)</td>
<td>77.5 (3266)</td>
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<tr>
<td>Prettrial use of ARB*</td>
<td>22.2 (929)</td>
<td>22.9 (963)</td>
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<tr>
<td>Beta-blocker</td>
<td>93.1 (3899)</td>
<td>92.9 (3912)</td>
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<tr>
<td>Diuretic</td>
<td>80.3 (3363)</td>
<td>80.1 (3375)</td>
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<td>Mineralocorticoid antagonist</td>
<td>54.2 (2271)</td>
<td>57.0 (2400)</td>
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<tr>
<td>Digitalis</td>
<td>29.2 (1223)</td>
<td>31.2 (1316)</td>
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<tr>
<td>ICD</td>
<td>14.9 (623)</td>
<td>14.7 (620)</td>
</tr>
<tr>
<td>Cardiac resynchronization therapy</td>
<td>7.0 (292)</td>
<td>6.7 (282)</td>
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</table>

*At the screening visit, 20 patients were not receiving the protocol-required treatment with an ACE inhibitor or an ARB, and 45 patients were taking both drugs. ACE=angiotensin-converting enzyme, ARB=angiotensin receptor blocker. ICD=implantable cardioverter defibrillator. McMurray JJ, et al. N Engl J Med. 2014;371(11):993-1004.

Please see ENTRESTO full Prescribing Information, including Boxed WARNING.
Rates of Hyperkalemia after Publication of the Randomized Aldactone Evaluation Study

David N. Juurlink, M.D., Ph.D., Muhammad M. Mamdani, Pharm.D., M.P.H.,
Douglas S. Lee, M.D., Alexander Kopp, B.A., Peter C. Austin, Ph.D.,
Andreas Laupacis, M.D., and Donald A. Redelmeier, M.D.
Prescriptions in Canada for Spironolactone

Hospitalizations for Hyperkalemia
The Bad News

**Rale of Hosp Death For Hyperkalemia**

*Figure 3.* Rate of In-Hospital Death Associated with Hyperkalemia among Patients Recently Hospitalized for Heart Failure Who Were Receiving ACE Inhibitors.

Each bar shows the rate of in-hospital death associated with hyperkalemia per 1000 patients during one four-month interval. The line beginning in the second interval of 1999 shows projected death rates derived from interventional ARIMA models, with 1 bars representing the 95 percent confidence intervals.
The Good News…

Figure 4. Rate of Readmission for Heart Failure among Patients Recently Hospitalized for Heart Failure Who Were Receiving ACE Inhibitors.

Each bar shows the rate of readmission for heart failure per 1000 patients during one four-month interval. The line beginning in the second interval of 1999 represents projected admission rates derived from interventional ARIMA models, with 1 bars representing the 95 percent confidence intervals.
2642 consecutive patients with potassium levels following Discharge for Acute Decompensated Heart Failure. Patients Followed up to 5 years. Effect of Potassium on survival was Evaluated.
Figure 1. A multivariable-adjusted analysis depicting the nonlinear association between the continuum of time-updated serum potassium values and the hazard ratios for all-cause mortality. The shape of the curve was determined by modeling serum potassium with a fractional polynomial with 4 degrees of freedom [−2 −1]. The shaded area represents the 95% confidence interval, and was centered at the median of potassium in the sample (4.3 mEq/L). Thus, any portion of the curve above the y-scale reference line of 1 is statistically significant. The omnibus P value for the entire trajectory was P=0.0012.
Association of Potassium Level on Mode of Death

Risk-gradient trajectory centered at median potassium value of 4.3 mEq/L.
Findings

• 10% of patients had significant K+ abnormalities
• In most patients, if they were hypokalemic or hyperkalemic, they remained so. 60%
• 50% of patients died over the course of study, 7.2% were from sudden death
• RR of hypokalemia was 2.35
• RR of hyperkalemia 1.55
Non absorbable agent that binds $K^+$ in exchange with $Ca^{++}$
A  Time to First Serum Potassium Level ≥5.5 mmol/liter

No. at Risk

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<th>Placebo</th>
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Week of Withdrawal Phase
Sodium Zirconium Cyclosilicate in Hyperkalemia

David K. Packham, M.B., B.S., M.D., Henrik S. Rasmussen, M.D., Ph.D., Philip T. Lavin, Ph.D., Mohamed A. El-Shahawy, M.D., M.P.H., Simon D. Roger, M.D., Geoffrey Block, M.D., Wajeh Qunibi, M.D.,

![Graph showing serum potassium levels over time with placebo and ZS-9, 10 g treatments, and significance marked with *P<0.05.](image)
Hyperkalemia

- 75 yo male with ischemic cardiomyopathy and diabetes, CKD 3
- 2 year Hx of HF with EF of 30%
- Treated with carvedilol, sacubitril/valsartan
- Creat 1.8, K+ 4.8, NTproBNP 2500
- Spironolactone added 25 mg a day
Hyperkalemia

- Labs checked 4 days later
- Creatinine 1.9, K+ 5.6
- EKG no changes
- Options?
Hyperkalemia

- Reduce dose of spironolactone
- Stop spironolactone
- Add Patiromer
The HF “Toolbox”
Conclusions

Potassium issues are common in patients with heart failure. Medications commonly used in HF cause both hypo and hyperkalemia.

Aldosterone blockers are very important in reduced EF HF and probably normal EF HF

Hyperkalemia can be life threatening and can limit EB therapies

New K+ binders exist and can reliably reduce K+ levels. No data as to whether this will lead to improved outcomes.