Guideline Concordance of Testing for Hyperkalemia and Kidney Dysfunction During Initiation of Mineralocorticoid Receptor Antagonist Therapy in Patients With Heart Failure

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Background—Mineralocorticoid receptor antagonists (MRA) reduce morbidity and mortality in heart failure with reduced ejection fraction but can cause hyperkalemia and acute kidney injury. Guidelines recommend measurement of serum potassium (K) and creatinine (Cr) before and serially after MRA initiation, but the extent to which this occurs is unknown.

Methods and Results—Using electronic data from 3 health systems 2005 to 2008, we performed a retrospective review of laboratory monitoring among 490 patients hospitalized for heart failure with reduced ejection fraction who were subsequently initiated on MRA therapy. Median age at time of MRA initiation was 73 years, and 37.1% were women. Spironolactone accounted for 99.4% of MRA use. Initial ambulatory MRA dispensing occurred at hospital discharge in 70.0% of cases. In the 30 days before MRA initiation, 94.3% of patients had a K or Cr measurement. Preinitiation K was >5.0 mmol/L in 1.4% and Cr ≥2.5 mg/dL in 1.7%. In the 7 days after MRA initiation among patients who remained alive and out of the hospital, 46.5% had no evidence of K measurement; by 30 days, 13.6% remained untested. Patient factors explained a small portion of postinitiation K testing (c-statistic, 0.67).

Conclusions—Although laboratory monitoring before MRA initiation for heart failure with reduced ejection fraction is common, laboratory monitoring after MRA initiation frequently does not meet guideline recommendations, even in patients at higher risk for complications. Quality improvement efforts that encourage the use of MRA should also include mechanisms to address recommended monitoring. (Circ Heart Fail. 2014;7:43-50.)

Key Words: aldosterone antagonist ■ clinical chemistry tests ■ guideline adherence ■ heart failure ■ hyperkalemia ■ mineralocorticoid receptor antagonists ■ safety ■ spironolactone
monthly for the first 3 months,16 a recommendation that has remained essentially unchanged in the 20099 and 201310 guideline updates. The European Society of Cardiology guidelines have also consistently recommended to check blood chemistry 1 and 4 weeks after starting/increasing dose.11,12 The extent to which these recommendations are being followed in routine practice has not been well characterized.13

Therefore, we set out to describe laboratory monitoring patterns for patients initiated on MRA in a large, multicenter, community-based cohort of adults with HFREF. Our aims were to (1) characterize patient selection for MRA therapy, (2) describe the frequency and results of preinitiation monitoring, (3) describe the frequency and timing of postinitiation monitoring, (4) identify factors associated with failure to perform recommended laboratory monitoring after MRA initiation, and finally (5) explore the association between early postinitiation testing and subsequent clinical outcomes.

Methods

Data Source

Participating health plans for the present study were Kaiser Permanente Colorado, Kaiser Permanente Northwest, and Fallon Community Health Plan.14,15 These health plans serve an ethnically and socioeconomically diverse population across varying clinical practice settings and geographically diverse areas. A Virtual Data Warehouse at each site served as a distributed standardized data resource comprised electronic data sets populated with linked demographic, administrative, ambulatory pharmacy, outpatient laboratory test results, and healthcare use data.16,17 For the present study, laboratory data were limited to the ambulatory setting because detailed inpatient clinical data were not consistently captured across study sites. Institutional review boards at participating sites approved the study, and waiver of consent was obtained because of the nature of the study.

Patient Population

All patients aged ≥21 years with diagnosed HF based on a hospitalization with a primary discharge diagnosis of HF between January 1, 2005 and December 31, 2008 using International Classification of Diseases, Ninth Edition (ICD-9) codes: 398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, and 428.x. Prior studies have shown a positive predictive value of ≥95% for HF when compared with Framingham clinical criteria.18–20 Assessments of left ventricular ejection fraction were ascertained for each patient with HF from echocardiograms, nuclear imaging modalities, and left ventriculography test results available from site-specific databases complemented by manual chart review. The measure obtained closest to the index date of study entry was used. We restricted the cohort to HFREF by requiring the summary left ventricular ejection fraction to be quantitatively ≤40% or qualitatively described as moderately or severely reduced.21 Patients without a documented left ventricular ejection fraction measurement were excluded (24.6%). Patients were required to have a new pharmacy dispensing of either spironolactone or eplerenone at any time after HF hospitalization, with no prior dispensing of these agents (Figure 1). MRA use was determined using filled outpatient prescriptions from health plan databases.

Covariates

Baseline covariates used to describe the cohort and perform multivariate modeling were chosen a priori based on presumed interactions with MRA therapy, previously published HF prognostic models, and availability within the Virtual Data Warehouse. We determined the presence of coexisting illnesses based on diagnoses or procedures using relevant ICD-9 codes, CPT procedure codes, and site-specific diabetes mellitus and cancer registries.17,21

Outcomes

Reflecting clinical guideline recommendations, we assessed serum potassium and creatinine measurement in the 30 days before MRA dispensing, the 7 days after MRA dispensing, and the 30 days after MRA dispensing. We also used a Kaplan–Meier estimate for time to the first serum potassium measure after MRA dispensing during available follow-up. Subjects were censored at the time they were hospitalized, died, disenrolled from the health plan, or reached the end of study follow-up (December 31, 2008). Hospitalizations were identified from each site’s Virtual Data Warehouse. Deaths were identified from hospital and billing claims databases, administrative health plan databases, state death certificate registries, and Social Security Administration files as available at each site.15,19

Statistical Analysis

We described baseline patient characteristics overall and stratified by serum potassium measure, no measure, or death/hospitalization in the 7 days after initial MRA dispensing. Continuous variables were ordinalized using cut points chosen based on clinically meaningful values. Missing covariate data were treated as a separate category. Statistical significance was evaluated using Wilcoxon rank-sum tests for continuous variables and χ2 or Fisher exact tests for categorical variables.

Step-wise multivariable logistic regression was used to examine the independent relationship between baseline characteristics and failure to perform laboratory monitoring in the week after MRA initiation, with model performance characterized using c-statistics and Nagelkerke pseudo-R2. Variable selection included predetermined key variables of clinical interest (age, sex, baseline serum potassium, and creatinine), as well as additional variables with significant univariate associations. Missing heart rate and blood pressure measures were imputed to the median.

Cox proportional hazards models were used to assess the relationship between testing 1 to 7 days after MRA initiation and the outcome of all-cause hospitalization or death 8 to 90 days after MRA initiation; variables included in the model were taken from the Yale readmission risk calculator.22 All analyses were conducted using SAS statistical software, version 9.1 (Cary, NC).
Table 1. Characteristics of Patients With Prior Hospitalization for Heart Failure With Reduced Left Ventricular Ejection Fraction at the Time of Initiation of a Mineralocorticoid Receptor Antagonist, Stratified by Death/Hospitalization, Serum Potassium Measure, or No Measure in the 7 Days After Initial MRA Dispensing

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Excluded Because of Death or Hospitalization Within 7 d (n=47; 9.6% of 490)</th>
<th>Eligible for 7-d Testing Comparisons (n=443; 90.4% of 490)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y; median (IQR)</td>
<td>76 (66–84)</td>
<td>73 (62–81)</td>
<td>74 (61–80)</td>
</tr>
<tr>
<td>Age categories, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤65 y</td>
<td>10 (21.3%)</td>
<td>76 (32.1%)</td>
<td>64 (31.1%)</td>
</tr>
<tr>
<td>65–74 y</td>
<td>10 (21.3%)</td>
<td>60 (25.3%)</td>
<td>45 (21.8%)</td>
</tr>
<tr>
<td>≥75 y</td>
<td>27 (57.5%)</td>
<td>101 (42.6%)</td>
<td>97 (47.1%)</td>
</tr>
<tr>
<td>Female sex, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤65 y</td>
<td>22 (46.8%)</td>
<td>87 (36.7%)</td>
<td>73 (35.4%)</td>
</tr>
<tr>
<td>LVEF, median (IQR)</td>
<td>0.25 (0.20, 0.33)</td>
<td>0.25 (0.20–0.33)</td>
<td>0.25 (0.20–0.30)</td>
</tr>
<tr>
<td>Missing LVEF</td>
<td>8 (17.0%)</td>
<td>82 (34.6%)</td>
<td>56 (27.2%)</td>
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<tr>
<td>Acute myocardial infarction</td>
<td>7 (14.9%)</td>
<td>39 (16.5%)</td>
<td>23 (11.2%)</td>
</tr>
<tr>
<td>Coronary artery bypass surgery</td>
<td>2 (4.3%)</td>
<td>17 (7.2%)</td>
<td>8 (3.9%)</td>
</tr>
<tr>
<td>Coronary stent or angioplasty</td>
<td>5 (10.6%)</td>
<td>30 (12.7%)</td>
<td>24 (11.7%)</td>
</tr>
<tr>
<td>Atrial fibrillation or flutter</td>
<td>9 (19.1%)</td>
<td>48 (20.3%)</td>
<td>33 (16.0%)</td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td>2 (4.3%)</td>
<td>16 (6.8%)</td>
<td>4 (1.9%)</td>
</tr>
<tr>
<td>Rheumatic valvular disease</td>
<td>7 (14.9%)</td>
<td>11 (4.6%)</td>
<td>5 (2.4%)</td>
</tr>
<tr>
<td>ICD</td>
<td>4 (8.5%)</td>
<td>19 (8.0%)</td>
<td>18 (8.7%)</td>
</tr>
<tr>
<td>Pacemaker</td>
<td>5 (10.6%)</td>
<td>23 (9.7%)</td>
<td>18 (8.7%)</td>
</tr>
<tr>
<td>Medical history, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic stroke or TIA</td>
<td>4 (8.5%)</td>
<td>16 (6.8%)</td>
<td>9 (4.4%)</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>16 (34.0%)</td>
<td>27 (11.4%)</td>
<td>26 (12.6%)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>27 (57.4%)</td>
<td>126 (53.2%)</td>
<td>97 (47.1%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>22 (46.8%)</td>
<td>117 (49.4%)</td>
<td>100 (48.5%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>9 (19.1%)</td>
<td>42 (17.7%)</td>
<td>38 (18.4%)</td>
</tr>
<tr>
<td>Diagnosed dementia</td>
<td>8 (17.0%)</td>
<td>25 (10.5%)</td>
<td>22 (10.7%)</td>
</tr>
<tr>
<td>Diagnosed depression</td>
<td>8 (17.0%)</td>
<td>51 (21.5%)</td>
<td>38 (18.4%)</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>20 (42.6%)</td>
<td>85 (35.9%)</td>
<td>80 (38.8%)</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>2 (4.3%)</td>
<td>9 (3.8%)</td>
<td>13 (6.3%)</td>
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<tr>
<td>Systemic cancer</td>
<td>12 (25.5%)</td>
<td>16 (6.8%)</td>
<td>18 (8.7%)</td>
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<tr>
<td>Medications at initial ambulatory MRA dispensing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spironolactone</td>
<td>47 (100%)</td>
<td>235 (99.2%)</td>
<td>205 (99.5%)</td>
</tr>
<tr>
<td>Eplerenone</td>
<td>0 (0%)</td>
<td>2 (0.8%)</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>Starting MRA dose, mg/24 h, mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤12.5</td>
<td>11 (23.4%)</td>
<td>92 (38.8%)</td>
<td>63 (30.6%)</td>
</tr>
<tr>
<td>25</td>
<td>20 (63.8%)</td>
<td>127 (53.6%)</td>
<td>132 (64.1%)</td>
</tr>
<tr>
<td>≥50</td>
<td>6 (12.8%)</td>
<td>18 (7.6%)</td>
<td>11 (5.3%)</td>
</tr>
<tr>
<td>Potassium supplement</td>
<td>18 (38.3%)</td>
<td>107 (45.1%)</td>
<td>75 (36.4%)</td>
</tr>
<tr>
<td>Loop diuretic</td>
<td>32 (68.1%)</td>
<td>187 (78.9%)</td>
<td>155 (75.2%)</td>
</tr>
<tr>
<td>Thiazide-type diuretic</td>
<td>4 (8.5%)</td>
<td>33 (13.9%)</td>
<td>19 (9.2%)</td>
</tr>
<tr>
<td>ACEI</td>
<td>22 (46.8%)</td>
<td>156 (65.8%)</td>
<td>135 (65.6%)</td>
</tr>
<tr>
<td>ARB</td>
<td>2 (4.3%)</td>
<td>24 (10.1%)</td>
<td>24 (11.7%)</td>
</tr>
<tr>
<td>β-blocker</td>
<td>26 (55.3%)</td>
<td>190 (80.2%)</td>
<td>164 (79.6%)</td>
</tr>
<tr>
<td>Digoxin</td>
<td>17 (36.2%)</td>
<td>104 (43.9%)</td>
<td>89 (43.2%)</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg, median (IQR)</td>
<td>121 (108–132)</td>
<td>122 (110–140)</td>
<td>120 (110–140)</td>
</tr>
</tbody>
</table>

(Continued)
Table 1. Continued

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Excluded Because of Death or Hospitalization Within 7 d (n=47; 9.6% of 490)</th>
<th>Eligible for 7-d Testing Comparisons (n=443; 90.4% of 490)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Testing ≤7 d From MRA Dispensing (n=237; 53.5% of 443)</td>
</tr>
<tr>
<td>Missing systolic BP</td>
<td>5 (10.6%)</td>
<td>11 (4.6%)</td>
</tr>
<tr>
<td>≤90</td>
<td>5 (10.6%)</td>
<td>13 (5.5%)</td>
</tr>
<tr>
<td>91–110</td>
<td>3 (6.4%)</td>
<td>58 (24.5%)</td>
</tr>
<tr>
<td>111–140</td>
<td>13 (27.7%)</td>
<td>103 (43.5%)</td>
</tr>
<tr>
<td>141–160</td>
<td>21 (44.7%)</td>
<td>40 (16.9%)</td>
</tr>
<tr>
<td>&gt;160</td>
<td>3 (6.4%)</td>
<td>12 (5.1%)</td>
</tr>
<tr>
<td>Heart rate, bpm, median (IQR)</td>
<td>80 (64, 96)</td>
<td>83.5 (72, 99)</td>
</tr>
<tr>
<td>Missing heart rate</td>
<td>5 (10.6%)</td>
<td>11 (4.6%)</td>
</tr>
<tr>
<td>Discharged to a facility location (nursing home, skilled nursing, rehab unit, or another hospital)</td>
<td>9 (3.8%)</td>
<td>12 (5.8%)</td>
</tr>
</tbody>
</table>

P values are from Fisher exact test and χ² test for categorical variables and Wilcoxon rank-sum for continuous variables and compare testing within 7 days to no testing within 7 days. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ICD, implantable cardioverter-defibrillator; IQR, interquartile range; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; and TIA, transient ischemia attack.

Results

In total, 490 patients with HFREF were initiated on MRA in the ambulatory setting. Median age was 73.6 years, and 37.1% were women (Table 1). Spironolactone accounted for 99.4% of MRA use and eplerenone for 0.6% of MRA use. The starting dose of MRA was 12.5 mg/d in 33.9%, 25 mg/d in 60.0%, and 50 mg/d in 7.1%. MRA was initially dispensed in 57.8% of patients at the time of a hospital discharge and within 1 to 7 days of a hospital discharge in an additional 12.2% of the cohort. Concomitant use of angiotensin-converting enzyme inhibitor or angiotensin receptor blocker was 73.5%; concomitant dispensing of both angiotensin-converting enzyme inhibitor and angiotensin receptor blocker in the setting of MRA initiation was 0.6%. The use of an MRA in the absence of a loop diuretic was 23.7%. The use of an MRA with concomitant use of oral potassium supplementation was 40.8%.

Preinitiation Laboratory Testing

In the 30 days before initial MRA dispensing, ambulatory serum potassium measurement was noted for 69.0%; an additional 25.3% of patients had no ambulatory monitoring but were hospitalized during this preinitiation period, presumably with laboratory monitoring during the hospitalization. Therefore, 5.7% of patients had no direct or indirect evidence of a serum potassium measurement in the 30 days before MRA initiation. Serum creatinine measurements closely paralleled serum potassium measures (absolute differences <1%). Among patients with available measurements, median preinitiation serum potassium was 4.1 mmol/L (interquartile range, 3.9–4.5); 1.2% (n=6) of patients had a potassium level above the recommended cutoff of 5.0 mmol/L on the measurement immediately preceding MRA initiation. Median preinitiation serum creatinine was 1.4 mg/dL (interquartile range, 1.1–1.6); 1.6% (n=8) had a creatinine level above the recommended cutoff of 2.5 mg/dL on the measurement immediately preceding MRA initiation (Table 2).

Postinitiation Laboratory Testing

Among the 443 patients who remained alive and out of the hospital (nonhospitalized and no urgent or emergency care visits) in the 7 days after MRA initiation, 46.5% (n=206) of patients did not have evidence of serum potassium measured 1 to 7 days after MRA dispensing. For the subset of patients with first ambulatory MRA dispensing occurring at or within 7 days of a hospital discharge, 43.6% (n=136/312) had no evidence of 7-day postinitiation serum potassium measurement; for those with first ambulatory MRA dispensing greater than a week after hospital discharge, 53.4% (n=70/131) had no evidence of 7-day postinitiation serum potassium measurement. After excluding patients (n=75) who were hospitalized, died, or had health plan enrollment termination in the 8 to 30 days after MRA initiation, 13.6% (n=50/368) of patients had no evidence of serum potassium measurement in the entire 30 days from MRA dispensing. For those patients who were monitored within 7 days and did not suffer death or hospitalization in the 30 days after MRA dispensing, the rate of a second potassium measurement in between days 8 and 30 was 67.5% (n=127/203). Figure 2 depicts a Kaplan–Meier analysis of time to potassium measurement, with censoring for hospitalization, death, or health plan disenrollment.

Factors Associated With Failure to Monitor

A combination of patient demographics, comorbidities, laboratory testing, vital signs, and medication use explained a relatively small portion of postinitiation K testing patterns (c-statistic, 0.67; Table 3).

Association With Postinitiation Monitoring and Subsequent Outcomes

In the 8 to 90 days after MRA initiation among patients that remained alive and out of the hospital in the first 7 days, death occurred in 6.2% (n=14/225) of those with 7-day serum potassium testing when compared with 6.1% (n=12/196) of those
without 7-day potassium testing (0.31 versus 0.29 deaths per person years, respectively; 0.97). All-cause hospitalization was also similar, with 1.70 hospitalizations per person years for patients with 7-day postinitiation serum potassium testing when compared with 1.61 hospitalizations per person years for patients without 7-day testing (0.41). Cox proportional hazards modeling was not statistically significant for the association between testing 1 and 7 days after MRA initiation and mortality or hospitalization 8 to 90 days postinitiation although was underpowered to assess small but clinically meaningful differences (adjusted hazards ratio, 1.18; 95% confidence interval, 0.83–1.62).

Discussion
In this study of patients with HFREF in managed care plans, laboratory monitoring after initiation of MRA frequently did not meet guideline recommendations. Although almost all patients had a baseline serum potassium and creatinine test (or a hospitalization with assumed testing) in the month before initiation of MRA, nearly half of patients had no evidence of a repeat serum potassium and creatinine measurement in the 7 days after initial MRA dispensing. Because of concerns about MRA-mediated hyperkalemia and renal dysfunction, particularly among patients outside of the narrow eligibility criteria and close supervision inherent in randomized controlled trials, such testing has been recommended since 2005, with all major heart failure clinical practice guidelines currently endorsing testing within at least a week of MRA initiation and again at 4 weeks.8–11,23 Not only were there gaps between observed and recommended postinitiation testing patterns but also testing had little association with risk (ie, lack of testing...
was not confined to the lowest risk patients). Finally, MRA initiation seemed to occur at a dose higher than recommended or with concomitant potassium supplementation in a significant minority of patients. These results highlight a need for education and systems of care that enhance appropriate safety monitoring, particularly if quality improvement initiatives and performance measures are implemented to increase the use of MRA in patients with HFREF.

The laboratory testing patterns seen here are concordant with older studies documenting suboptimal monitoring after initiation of MRA and other high-risk medications in general populations. In a study looking at laboratory evaluation among all ambulatory patients dispensed spironolactone in 1999 to 2000 within 10 health maintenance organizations (regardless of indication), 27.7% of patients had not had a follow-up test for potassium and creatinine for the next 13 months. Contemporary patterns of laboratory monitoring have not been described in detail for HFREF populations and speak to the novelty of our findings.

The results presented here do not address the reasons for nonadherence to monitoring recommendations for MRA use in HFREF. Prior study has shown that a computerized system of monitoring alerts managed by pharmacists increased the number of patients who received laboratory safety monitoring of drug therapy; in contrast, laboratory monitoring alerts within a computerized physician order entry system have not improved monitoring. These data suggest that physicians may not be best positioned to order follow-up testing. Furthermore, our study assessed the actual performance of laboratory testing, not the intent of prescribing clinicians to obtain such testing in follow-up. The high rate of preinitiation testing (the absence of which may allow a provider not to prescribe MRA) but subsequently low postinitiation testing (over which a provider has less control) suggests that many gaps in recommended testing may be related to system execution and patient adherence with such testing.

Whether greater monitoring may improve safety and help increase the benefit of MRA use in patients with HFREF in real-world remains to be determined. Theoretically, improvements in adherence to guideline recommended laboratory monitoring can lead to pre-emptive changes in MRA dosing, thereby avoiding some unnecessary adverse events. Yet, interventions that improve laboratory monitoring have not necessarily translated into cost-effective mechanisms to improve clinical outcomes, particularly if not concentrated among high-risk patients and targeted to the healthcare providers best suited to implement suggested monitoring.

The policy implications of laboratory testing related to MRA use are important. Appropriate MRA use is the lowest of major recommended therapies for HFREF. Yet, a joint report from the American College of Cardiology/American Heart Association Task Force on Performance Measures and the American Medical Association Physician Consortium for Performance Improvement decided not to include MRA use: “…treatment with aldosterone receptor antagonists was considered but not developed because of the large number of patients excluded from the denominator because of renal insufficiency or hyperkalemia before or during treatment with these agents. In addition, the development of serious renal failure or hyperkalemia in large numbers of patients might be an unintended consequence of the broad implementation of such a measure.” Development of effective systems for laboratory monitoring before and after MRA initiation may assuage these concerns, thereby allowing for responsible MRA performance measures that help larger numbers of patients with HFREF in real-world realize the benefits of MRA seen in randomized trials.

### Potential Limitations

Insured populations in our participating health plans may not be fully representative of the general US population or international populations. Nevertheless, the demographic diversity represented across 3 geographically diverse health plans, as well as the community-based nature of healthcare delivery,
suggest that findings from our cohort are likely to be highly
generalizable to patients with HFREF in real-world practice
settings. The data used here to define MRA initiation come
from the dispensing date of prescribed MRA, which may mis-
classify some patients who start their drug at a later date or
who do not end up taking it at all. Laboratory testing may
occur outside the healthplan electronic data capture either at
distant sites or at contract hospitals; however, the potential for
such missing data is small as patients are financially discour-
aged from out-of-system testing and our methods accounted
for non-network hospitalizations. Most patients initiating
ambulatory MRA within a day of hospital discharge presum-
ably had been started on MRA during hospitalization with
laboratory monitoring during the hospital course; regardless,
such patients are relatively high risk for ongoing serum potas-
sium and creatinine changes after discharge, and thus multiple
organizations now recommend clinical follow-up and labora-
tory testing within a week after any HF hospital discharge.

Conclusions
Laboratory monitoring after initiation of an MRA in real-world
practice frequently does not meet guideline recommendations.
Given the known risks of MRA, quality improvement efforts
that encourage the use of MRA for HFREF should also con-
sider effective mechanisms to ensure appropriate monitor-
ing. The extent to which poor monitoring reduces safety and
explains the lack of benefit for MRA seen in observational
studies should be further evaluated.

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Disclosures
None.

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patients prescribed spironolactone: are we monitoring for hyperkalemia?


**CLINICAL PERSPECTIVE**

Aldosterone/mineralocorticoid receptor antagonists (MRA)—spironolactone and eplerenone—reduce hospitalization and death among patients with heart failure and reduced ejection fraction. They can also cause hyperkalemia and renal insufficiency. Therefore, clinical practice guidelines endorse measurement of serum potassium (K) and creatinine (Cr) before, 1 week after, and 4 weeks after starting an MRA, with changes to prescribing recommended for hyperkalemia and renal insufficiency. To investigate the extent to which such monitoring occurs in routine clinical practice, we identified 490 patients from 3 large health systems who were previously hospitalized with heart failure and reduced ejection fraction and then initiated on MRA. In the 30 days before MRA initiation, 5.7% of patients had no evidence of K or Cr measurement, 1.4% had K above the recommended level of 5.0 mmol/L, and 1.7% had Cr above the recommended level of 2.5 mg/dL. Among patients who remained alive and out of the hospital after MRA initiation, by 7 days 46.5% were untested for K and Cr; by 30 days, 13.6% remained untested. Testing was minimally related to patient factors associated with complications. Given the known risks of MRA, quality improvement efforts that encourage the use of MRA for heart failure and reduced ejection fraction should also consider effective mechanisms to ensure appropriate monitoring. The extent to which lapses in monitoring leads to potentially avoidable adverse events and explains the lack of effectiveness for MRA seen in observational studies warrants further study.
Guideline Concordance of Testing for Hyperkalemia and Kidney Dysfunction During Initiation of Mineralocorticoid Receptor Antagonist Therapy in Patients With Heart Failure

Larry A. Allen, Susan M. Shetterly, Pamela N. Peterson, Jerry H. Gurwitz, David H. Smith, David W. Brand, Diane L. Fairclough, John S. Rumsfeld, Frederick A. Masoudi and David J. Magid

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