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Consistency of Laboratory Monitoring During Initiation of Mineralocorticoid Receptor Antagonist Therapy in Patients With Heart Failure

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Introduction

Mineralocorticoid receptor antagonists (MRAs) are a cornerstone of heart failure therapy but have a risk of hyperkalemia. Clinical guidelines recommend close monitoring of renal function and electrolyte levels throughout the course of therapy.[1] No large studies have examined whether laboratory monitoring occurs routinely in community practice.

Methods

Using the Centers for Medicare & Medicaid Services Virtual Research Data Center to access claims and summary data for beneficiaries from 10 eastern states who were alive and enrolled in fee-for-service Medicare and in the Medicare Part D prescription drug benefit for the entire 2011 calendar year, we analyzed a cohort with prevalent heart failure who newly initiated MRA therapy. We identified prevalent heart failure using the Chronic Conditions Data Warehouse midyear indicator; we identified incident MRA use by the presence of a Part D claim for eplerenone or spironolactone between May 1 and September 30, 2011, with no such claims between January 1 and April 30, 2011.[2] Outcomes included measurement of serum creatinine and potassium levels before and after MRA initiation, as suggested in guidelines. We defined appropriate testing as a claim for a specific test or laboratory panel including creatinine and potassium within 120 days before initiation, 2 or more

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measurements during the early post-initiation period (days 1 through 10), and 3 or more measurements during the extended post-initiation period (days 11 through 90). We counted each hospitalization as 1 test during that period. If the initial MRA prescription fill occurred within 3 days after discharge, we considered the patient to have both in-hospital initiation and 1 test in early post-initiation follow-up.

We summarized laboratory testing using frequencies with percentages. We used multivariable logistic regression to estimate associations between patient characteristics and laboratory monitoring, adjusting for demographic characteristics and comorbid conditions. We used a 2-sided $P < .05$ to establish statistical significance and report 95% CIs. We used SAS version 9.3 (SAS Institute Inc) for all analyses. The institutional review board of the Duke University Health System approved the study and granted a waiver of consent.

Results

The study population included 10,443 Medicare beneficiaries with heart failure and incident MRA therapy. Mean age was 78.6 years (SD, 7.8), 4142 patients (39.6%) were men, and 8354 (80%) were white. Chronic kidney disease was present in 4744 patients (45.4%), and 5571 patients (53.3%) were taking an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker. Combined, 756 patients (7.2%) received appropriate testing before and after MRA initiation (Table 1). After initiation, 1384 patients (13.3%) and 3122 patients (29.9%) received appropriate testing in early and extended follow-up, respectively. In contrast, 5782 (55.4%) and 2328 (22.3%) received no testing in early or extended follow-up, respectively.

Atrial fibrillation, anemia, chronic kidney disease, chronic obstructive pulmonary disease, hypothyroidism, osteoporosis, and use of diuretics were associated with a greater likelihood of appropriate laboratory testing in all periods (Table 2).

Discussion

Frequent laboratory monitoring of patients with heart failure during MRA initiation is supported by clinical trial evidence and endorsed in guidelines, but we observed low rates of monitoring in clinical practice.[1,3,4] The landmark trials of MRAs in heart failure showed MRAs significantly reduced mortality and cardiovascular readmission compared with placebo.[3,4] However, an analysis of community practice found similar outcomes among patients treated or not treated with an MRA.[5] One possible explanation may be less rigorous monitoring outside clinical trial settings, which may increase risks of adverse events associated with MRAs.[6] Closing the gap between the efficacy and effectiveness of MRAs in heart failure will require clinicians to address this issue. Quality improvement initiatives to improve appropriate laboratory monitoring are needed.

Limitations of our study include the limited population, possible inaccurate claims data, and likely unmeasured confounders. In addition, we only captured data on whether and when laboratory testing occurred but not indications for testing or uncompleted tests.

In conclusion, rates of appropriate laboratory monitoring after MRA initiation were low, and greater attention to appropriate laboratory monitoring is needed.

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Table 1

Observed Laboratory Testing of Potassium and Creatinine Levels Among Patients Initiating Mineralocorticoid Receptor Antagonist Therapy for Heart Failure

Testing	Patients, No. (%) (N = 10,443)
Pre-initiation testing (120 days before drug initiation)	
Appropriate pre-initiation testing[a]	9564 (91.6)
No pre-initiation testing	879 (8.4)
Early post-initiation testing (1–10 days after drug initiation)[b]	
Appropriate early post-initiation testing	1384 (13.3)
Any early post-initiation testing	4661 (44.6)
No early post-initiation testing	5782 (55.4)
Extended post-initiation testing (11–90 days after drug initiation)[c]	
Appropriate extended post-initiation testing	3122 (29.9)
Any extended post-initiation testing	8115 (77.7)
No post-initiation testing	2328 (22.3)
All appropriate testing	756 (7.2)
No pre- or post-initiation testing	280 (2.7)

[a]Appropriate pre-initiation testing was defined by the presence of at least 1 laboratory claim (or hospitalization) within 120 days before drug initiation.

[b]Appropriate early follow-up testing was defined by the presence of 2 laboratory claims (or hospitalizations, or 1 laboratory claim plus hospital discharge within 3 days before initial outpatient prescription fill) within 10 days after drug initiation.

[c]Appropriate extended follow-up testing was defined by the presence of 3 laboratory claims (or hospitalizations) within 11 to 90 days after drug initiation.

Table 2

Patient Characteristics Associated With Appropriate Laboratory Testing of Potassium and Creatinine

Variable	Appropriate Testing, Risk Ratio (95% CI)[a]			
	Pre-Initiation	Early Post-Initiation	Extended Post-Initiation	All Testing
Age, per 5 years	1.00 (1.00–1.01)	0.98 (0.94–1.01)	0.98 (0.96–1.00)	0.95 (0.91–1.00)
Male	0.98 (0.97–1.00)	1.03 (0.91–1.16)	1.04 (0.97–1.12)	1.02 (0.86–1.21)
Race				
Black	1.00 (0.98–1.01)	0.89 (0.76–1.03)	0.93 (0.85–1.01)	0.89 (0.72–1.10)
White	1.00 [Reference]	1.00 [Reference]	1.00 [Reference]	1.00 [Reference]
Other/unknown	0.95 (0.92–0.98)	0.77 (0.60–0.98)	0.77 (0.67–0.89)	0.70 (0.49–0.99)
Medical history				
Acquired hypothyroidism	1.04 (1.02–1.05)	1.22 (1.09–1.37)	1.26 (1.18–1.34)	1.33 (1.14–1.55)
Anemia	1.05 (1.04–1.07)	1.21 (1.09–1.36)	1.36 (1.27–1.46)	1.45 (1.23–1.71)
Asthma	1.01 (0.99–1.02)	1.04 (0.91–1.20)	1.07 (0.99–1.16)	1.02 (0.84–1.23)
Atrial fibrillation	1.03 (1.01–1.04)	1.35 (1.22–1.49)	1.22 (1.15–1.30)	1.50 (1.30–1.73)
Benign prostatic hyperplasia	1.03 (1.02–1.05)	1.12 (0.95–1.32)	1.03 (0.94–1.14)	1.22 (0.98–1.52)
Cancer	1.03 (1.02–1.05)	1.06 (0.92–1.22)	1.16 (1.08–1.26)	1.14 (0.95–1.38)
Chronic kidney disease	1.04 (1.03–1.05)	1.40 (1.26–1.55)	1.48 (1.39–1.57)	1.83 (1.58–2.13)
Chronic obstructive pulmonary disease	1.03 (1.02–1.04)	1.27 (1.14–1.41)	1.07 (1.01–1.14)	1.29 (1.12–1.49)
Dementia, Alzheimer disease, or related condition	1.00 (0.99–1.02)	1.01 (0.89–1.14)	1.00 (0.94–1.08)	1.01 (0.86–1.20)
Depression	1.01 (1.00–1.02)	1.02 (0.91–1.15)	1.07 (1.00–1.14)	1.06 (0.90–1.24)
Diabetes mellitus	1.04 (1.02–1.05)	0.97 (0.87–1.08)	1.13 (1.06–1.21)	1.05 (0.91–1.22)
Hyperlipidemia	1.05 (1.03–1.07)	1.05 (0.93–1.19)	1.09 (1.01–1.17)	1.16 (0.97–1.39)
Hypertension	1.13 (1.09–1.17)	1.29 (1.02–1.64)	1.18 (1.02–1.36)	1.13 (0.81–1.59)
Ischemic heart disease	1.00 (0.98–1.02)	1.22 (1.05–1.43)	1.11 (1.02–1.21)	1.23 (0.98–1.53)
Osteoporosis	1.03 (1.01–1.04)	1.17 (1.01–1.36)	1.10 (1.01–1.20)	1.31 (1.07–1.60)
Rheumatoid arthritis or osteoarthritis	1.00 (0.99–1.01)	0.83 (0.75–0.93)	1.02 (0.96–1.08)	0.87 (0.75–1.00)
Stroke	1.02 (1.00–1.03)	1.10 (0.95–1.28)	1.02 (0.94–1.12)	1.08 (0.88–1.33)
Other medications				
ACE inhibitor or ARB	1.02 (1.01–1.03)	1.16 (1.05–1.28)	1.04 (0.99–1.11)	1.05 (0.91–1.21)
β-Blocker	1.02 (1.01–1.03)	1.31 (1.17–1.47)	1.03 (0.96–1.10)	1.14 (0.98–1.33)
Diuretic	1.03 (1.02–1.05)	1.64 (1.41–1.91)	1.31 (1.21–1.42)	1.78 (1.44–2.21)

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker.

[a]Risk ratio of appropriate testing in multivariable analysis. Reference categories: age (per 5 year increase over age 65), sex (male vs female), race (vs white race), medical history (vs absence of condition), medications (vs no use of the medication). Testing includes allowances for hospitalizations.