Utilization of Spironolactone in Patients with Reduced or Preserved Ejection Fraction Heart Failure

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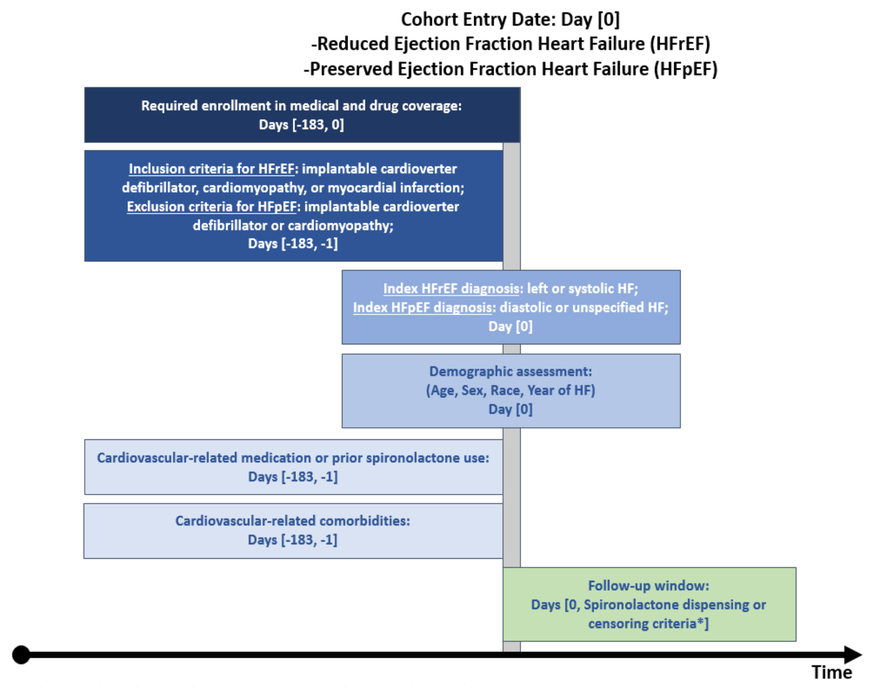
BACKGROUND

- Spironolactone is an aldosterone antagonist indicated for the management of heart failure with reduced ejection fraction (HFrEF).
- Consensus-based guidelines recommend the use of spironolactone in the management of heart failure with preserved ejection fraction (HFpEF) based on evidence from the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) trial.
- Patients randomized to spironolactone in the TOPCAT trial had a lower incidence of heart failure related hospitalizations when compared to placebo (hazard ratio, 0.83; 95% CI, 0.69 to 0.99, P=0.04).
- Our objective was to characterize the real-world utilization of spironolactone in patients with HFrEF and HFpEF separately in the U.S. FDA Sentinel System.

METHODS

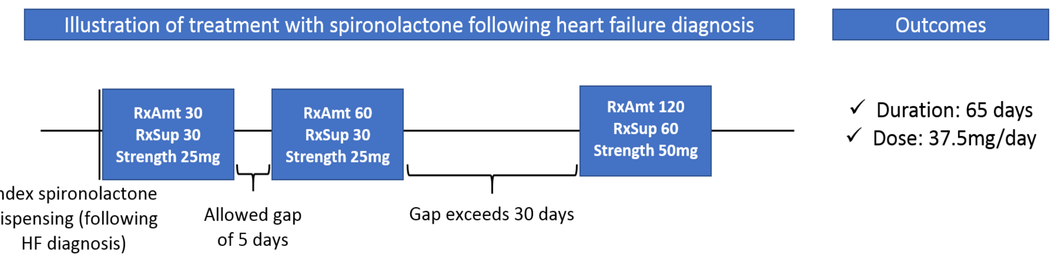
- Descriptive cohort study conducted using data from the FDA's Sentinel System.
  - Distributed network of 16 data partners in the U.S.: large national insurers, integrated delivery networks, a state Medicaid, 100% Medicare fee for service
- Cohort selection period: July 1, 2010 – September 30, 2018
- Patients entered the cohort on a diagnosis of HFrEF or HFpEF and were followed until the earliest occurrence of a dispensing of spironolactone, disenrollment, death, or data end date.
- Definition of HFrEF:
  - Left or systolic heart failure on the index date with no evidence of diastolic or combined heart failure on the same date
  - Baseline history of cardiomyopathy or myocardial infarction or an implantable cardioverter defibrillator
- Definition of HFpEF:
  - Diastolic or unspecified (rheumatic or hypertensive) heart failure on the index date with no evidence of left, systolic, or combined heart failure on the same date
  - No baseline history of cardiomyopathy or an implantable cardioverter defibrillator
- Utilization of spironolactone (dose and duration) was characterized among those treated with spironolactone following their heart failure diagnosis.
- All analyses were conducted using the Sentinel Query Request Package, version 9.0.1.

Figure 1. Study Design Schematic



*censoring criteria: spironolactone dispensing, disenrollment, death, or data end date

Figure 2. Characterization of Spironolactone Use



RESULTS

Table 1. Select Demographic and Clinical Characteristics of HFrEF and HFpEF Patients in the Sentinel System between July 2010 and September 2018

	HFrEF	HFpEF
Characteristic[1]	**%/Std Dev**	**%/Std Dev**
Number of unique patients	2,009,529	9,257,514
Demographics		
Mean Age	73.8±12.1	73.0±12.1
Age: 0-17	<0.1%	<0.1%
Age: 18-44	2.4%	3.0%
Age: 45-64	17.7%	18.2%
Age: 65+	79.9%	78.8%
Gender (Female)	42.2%	57.3%
Gender (Male)	57.8%	42.7%
Spironolactone use in the prior 183 days	5.7%	1.4%
History of cardiovascular-related medication use in the prior 183 days:		
Angiotensin-converting enzyme inhibitors	43.0%	33.7%
Beta blockers	71.3%	48.8%
Digoxin	12.0%	4.0%
Hydralazine	7.5%	4.2%
Loop diuretics	53.9%	27.9%
Mineralocorticoid receptor antagonists (eplerenone)	0.8%	0.1%
Nitrates	20.9%	10.0%
Potassium-sparing diuretics	9.7%	4.8%
Thiazide diuretics	16.4%	25.6%
History of heart failure related comorbidities in the prior 183 days:		
Atrial fibrillation or flutter	47.0%	20.9%
Diabetes mellitus	49.9%	40.7%
Hyperkalemia	12.0%	4.5%
Hyperlipidemia	72.6%	61.6%
Hypertension	88.7%	81.8%
Hypertensive nephropathy	32.5%	13.7%
Hypotension	18.1%	5.9%
Myocardial infarction	34.7%	3.6%
Nephropathy	54.4%	30.0%
Obesity	20.5%	15.9%
Other dysrhythmias	48.4%	19.0%
Renal disorders	40.4%	21.4%
Rheumatic heart disease	16.4%	4.9%
Valve disorders	20.7%	7.8%

[1]All metrics are based on total number of episodes per group, except for sex and race which are based on total number of unique patients.

Figure 3. Spironolactone Initiation Following Diagnosis of Heart Failure

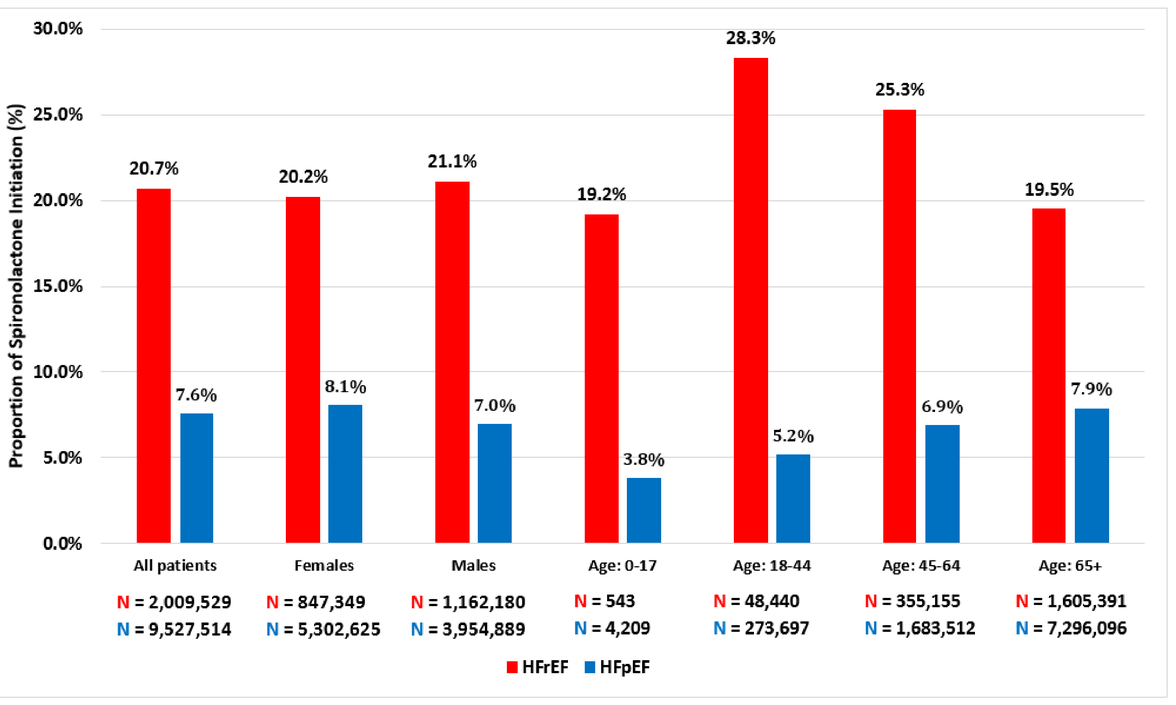


Table 2. Spironolactone Use Following Diagnosis of Heart Failure

Measures of Utilization	HFrEF	HFpEF
Median time to first spironolactone dispensing following HF diagnosis (in days)	90 (IQR: 19 – 385)	286 (IQR: 57 – 851)
Median duration of first continuous spironolactone treatment episode (in days)	120 (IQR: 44 – 321)	114 (IQR: 32 – 301)
Median average daily dose (mg per day) in the first continuous spironolactone treatment episode	25 (IQR: 25 – 25)	25 (IQR: 25 – 45)

DISCUSSION

- Lower initiation of spironolactone following HFpEF compared to HFrEF; but similar dosing and duration of the first continuous spironolactone episode.
- Plausible reasons for low use include limited evidence supporting effectiveness of spironolactone in HFpEF and the need for careful monitoring of potassium and renal function.
- This is the first study to characterize the use of spironolactone in a large, demographically and geographically diverse database in the U.S.
- Our findings must be interpreted with caution owing to the nature of administrative health claims and pharmacy dispensing data.

ACKNOWLEDGEMENTS

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