

Testing the Waters: Comparison of Diuresis Patterns in Heart Failure with Reduced versus Preserved Ejection Fraction

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Background

- An estimated 5.7 million Americans have heart failure, which is projected to surpass 8 million by 2030.¹
- Heart failure with reduced ejection fraction (HFrEF) is characterized by impaired ventricular ejection during systole, often defined as an ejection fraction of 40 percent or less, whereas heart failure with preserved ejection fraction (HFpEF) involves impaired filling during diastole.²
- Therapies demonstrated to decrease mortality in HFrEF, such as angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, beta-adrenergic blockers, and aldosterone antagonists have not been shown to have the same benefit in HFpEF.²
- Most clinical trials of patients with acute decompensated heart failure (ADHF) and congestive symptoms do not differentiate between these two groups. As a result, management of congestion is generally the same, with diuretics being a cornerstone of therapy.
- Considering the differences in pathophysiology and outcomes of chronic heart failure therapies among these two groups, it is plausible that diuretic therapy during an acute decompensation impacts HFrEF and HFpEF patients differently.

Objective and Hypothesis

- Objective:** to compare diuretic response among HFrEF and HFpEF patients in the setting of acute decompensated heart failure.
- Hypothesis:** HFpEF patients will require less diuretic to achieve the same response as HFrEF patients

Methods

- Study design:** retrospective cohort study
- Data collected via chart review of an electronic medical record system
- Primary endpoint:** cumulative diuretic response over first 72 hours of hospitalization, measured as mg of loop diuretic in intravenous (IV) furosemide equivalents per net fluid loss in mL
- Secondary endpoints:** diuretic dose, urine output, net fluid loss, adverse drug events (acute kidney injury, hypokalemia, hypomagnesaemia, hyponatremia), change in serum creatinine (SCr), change in weight, hospitalization characteristics (IV inotrope requirement, IV vasodilator requirement, length of hospitalization, in-hospital mortality, progression to renal replacement therapy (RRT))
- Statistical analyses performed using chi-square/Fischer's exact and t-test

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none"> Age 18-89 Diagnosis of ADHF Documented ejection fraction within 72 hours of admission or 6 months prior to hospitalization Admission to Primary Cardiology Service or Advanced Heart Failure Service at University of Maryland Medical Center within past 2 years At least 1 dose of IV loop diuretic given on admission 	<ul style="list-style-type: none"> Death within 72 hours of hospital admission Cirrhosis Current treatment with spironolactone > 50 mg or eplerenone >100 mg ESRD, estimated GFR < 10 mL/min, or use of renal replacement therapy during initial 72 hours

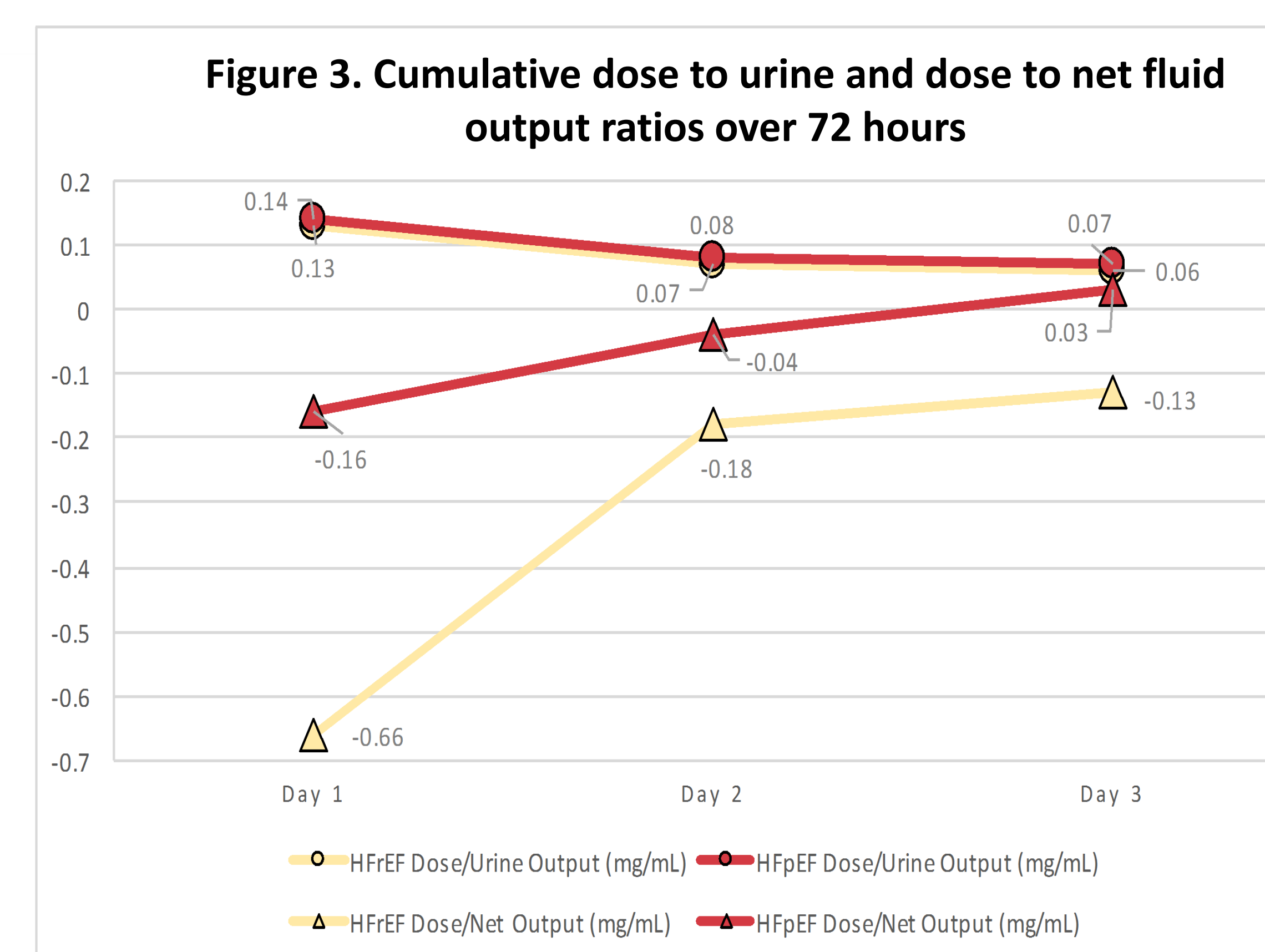
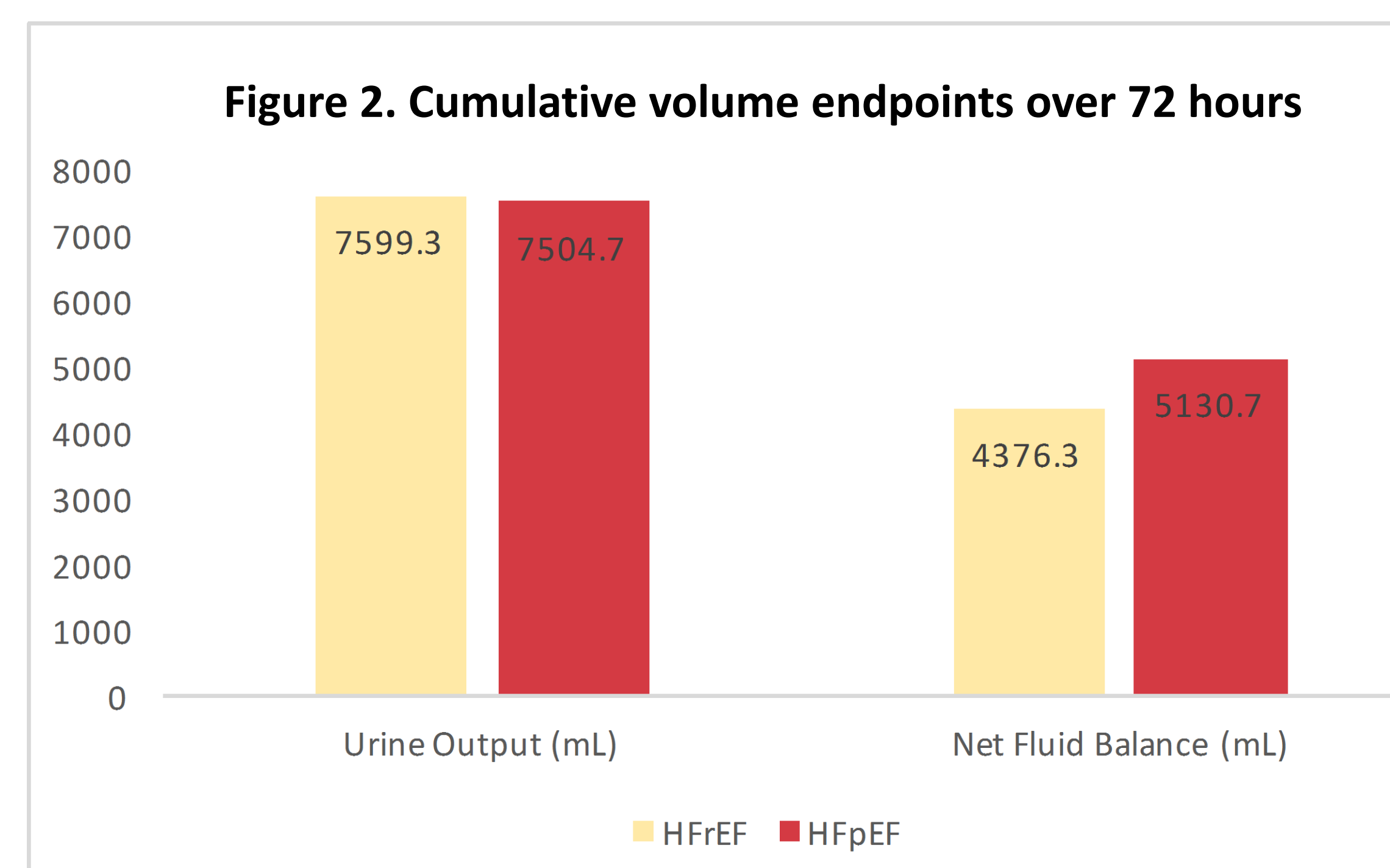
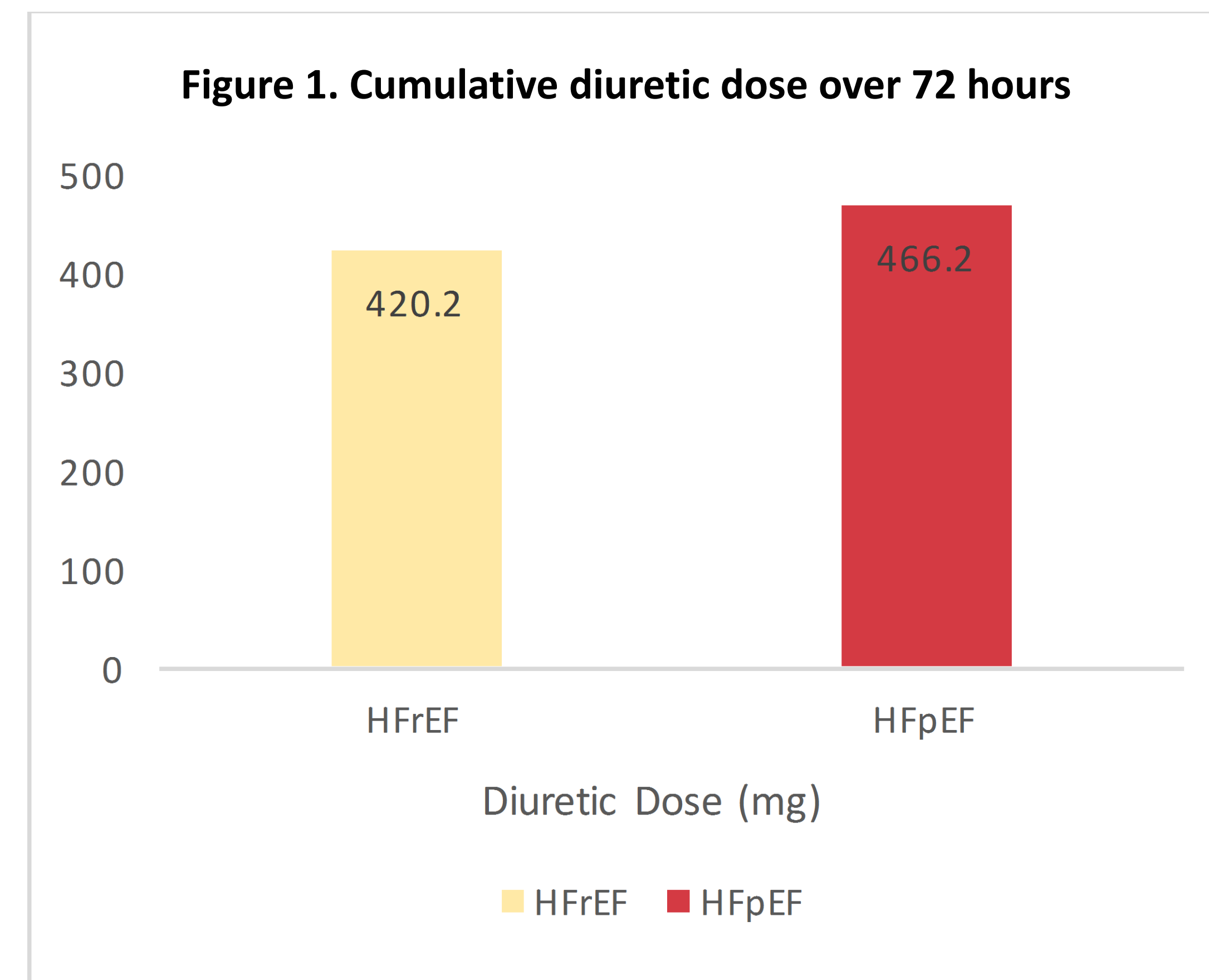
Results

Table 1. Baseline Characteristics			
Characteristics	HFrEF (n=30)	HFpEF (n=30)	p-value
Age	56.1 (13.7)	65.1 (9.8)	0.005
Gender, Male (%)	21 (70.0%)	14 (46.7%)	0.067
Race			
White	18	13	0.266
Black	12	14	
Other	0	3	
History			
Atrial fibrillation	9	10	0.781
Myocardial infarction	14	11	0.432
Diabetes mellitus	9	13	0.284
Chronic kidney disease	12	13	0.793
Ejection fraction	20.4 (8.6)	59.6 (10.6)	<0.001
Ventricular failure			
Left	10	7	0.001
Right	0	12	
Biventricular	20	11	
Heart failure etiology			
Ischemic	13	4	0.002
Non-ischemic	10	6	
Other/unknown	7	20	
NYHA Class			
II	1	1	0.514
III	7	4	
IV	5	3	
Unknown	17	22	
Home medications			
Loop diuretic	19	23	0.260
Thiazide-type diuretic	4	6	0.488
ACEi/ARB/ARNI	13	14	0.795
Beta blocker	20	10	0.010
Aldosterone antagonist	15	6	0.015
Nitrates/hydralazine	2	2	>0.99
IV inotropes	3	1	0.612
Home loop diuretic			
Furosemide	15	11	0.061
Bumetanide	1	7	
Torsemide	3	6	
Home loop diuretic dose (mg/d)*	88.1 (45.6)	110 (62.6)	0.204
Vitals/laboratories			
Systolic blood pressure	120.2 (17.9)	133.4 (23.8)	0.019
Serum sodium	135.6 (3.8)	136.5 (6.2)	0.515
Serum creatinine	1.5 (0.8)	1.7 (0.9)	0.540
NT-proBNP	11928 (12114)	7534 (6377)	0.169
Weight	92.0 (33.0)	105.0 (39.1)	0.170

*In furosemide equivalents

Results (continued)

Table 2. Secondary Outcomes			
Outcomes	HFrEF (n=30)	HFpEF (n=30)	p-value
Adverse drug events			
Acute kidney injury	8	4	0.197
Hypokalemia	27	25	0.706
Severe hypokalemia	14	8	0.108
Hypomagnesemia	13	12	0.793
Severe hypomagnesemia	1	0	>0.99
Severe hyponatremia	0	2	0.492
Maximum change in SCr	0.2 (0.4)	0.1 (0.4)	0.418
Change in weight	-2.5 (3.6)	-1.7 (4.8)	0.261
Hospitalization			
Right heart catheterization	18	16	0.602
IV inotrope requirement	13	8	0.176
IV vasodilator requirement	4	2	0.671
Length of stay	11.7 (15.2)	15.0 (14.3)	0.393
In-hospital mortality	0	3	0.237
Progression to RRT	1	5	0.195



Conclusions

- Baseline characteristics were generally similar between the two groups, with the exceptions that HFpEF patients were older, had higher systolic blood pressure at presentation, and were more likely to have right ventricular failure.
- A trend towards greater diuretic response in HFpEF patients was observed, but the difference between the two groups was not statistically significant. However, standard deviations were very wide for some variables, including diuretic dose and net fluid balance (both of which were used to determine the primary outcome).
- The incidence of adverse effects appeared to be similar between the two groups.
- A more adequately powered study with more patients is necessary to verify the results of this small pilot study.
- Based on the results of this study, we cannot conclude that HFrEF and HFpEF patients with ADHF respond differently to intravenous loop diuretic therapy.

Bibliography

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