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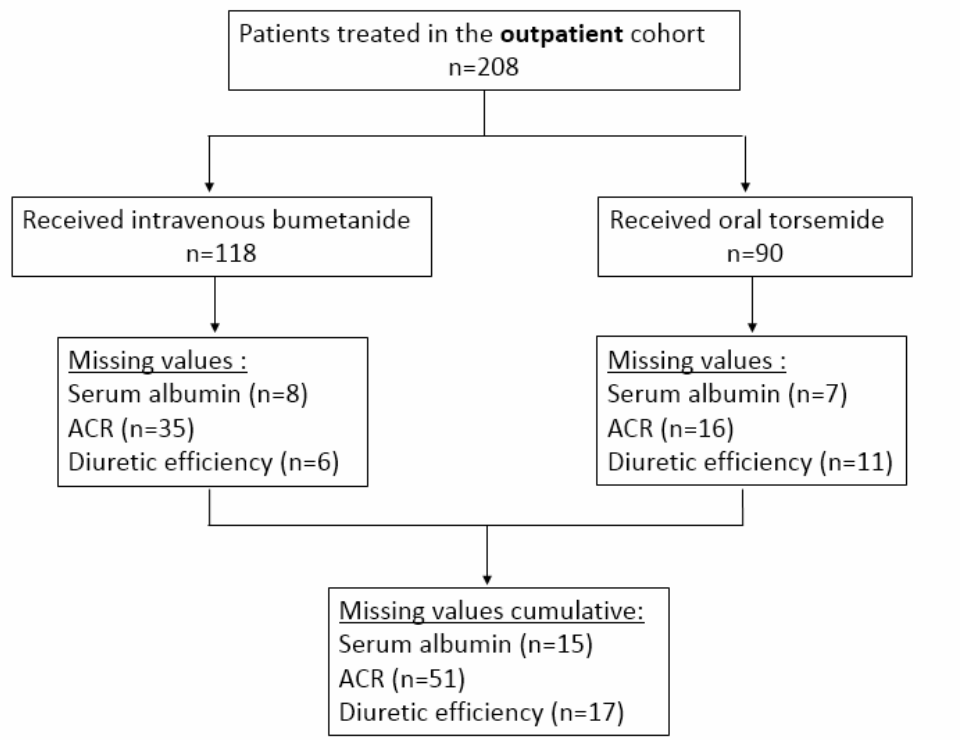
Supplemental Methods Section

Supplemental Table 1: Baseline Patient Characteristics According to Serum Albumin in the **inpatient** cohort. Values reflect mean (±SD) if linearly distributed or number (percentage) if categorical.

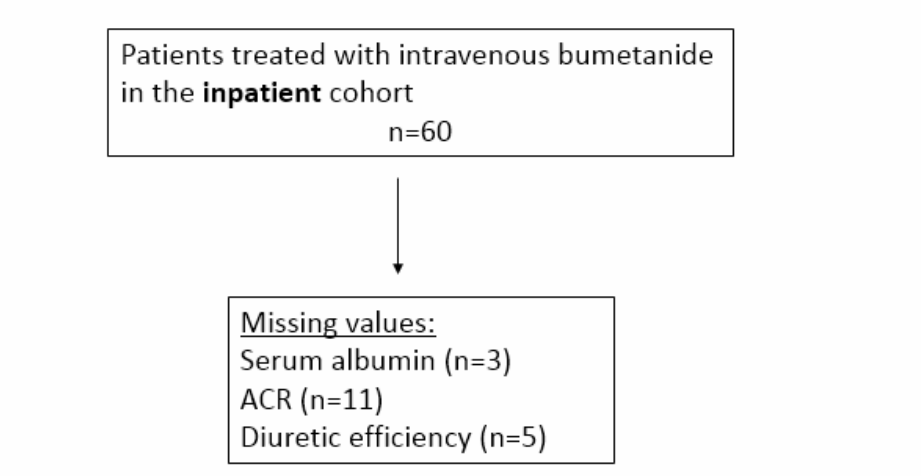
	Serum Albumin < median (n=27)	**Serum Albumin ≥ median (n=30)**
Demographics		
Age (year)	59 ± 15	57 ± 12
Gender Female, n (%)	8 (30)	11 (37)
Never Smoker, n (%)	8 (30)	15 (54)
Comorbidities		
Diabetes, n (%)	15 (56)	12 (40)
Stroke, n (%)	4 (15)	2 (7)
CAD, n (%)	12 (44)	10 (33)
Arrhythmia, n (%)	19 (70)	20 (67)
Valvular heart disease, n (%)	7 (26)	12 (40)
Ejection Fraction %	27 ± 18	25 ± 14
Hypertension, n (%)	19 (70)	16 (53)
Sleep apnea, n (%)	6 (22)	8 (27)
Baseline laboratory values		
Serum albumin (g/dL)	3.1 ± 0.4	3.9 ± 0.3
Urine albumin/Creat ratio, ACR (mg/g Cr)	90 (IQR 23-560)	23 (IQR 9-85)
Serum creatinine (mg/dL)	1.7 ± 0.8	1.7 ± 0.9
eGFR, CKD-EPI (ml/min/1.73m^2)	51 ± 27	56 ± 30
BUN/Creatinine ratio	26 ± 10	25 ± 10
Serum Sodium (mEq/L)	136 ± 4	135 ± 3
Serum Potassium (mEq/L)	4.1 ± 0.4	3.9 ± 0.6
Serum Chloride (mEq/L)	97 ± 5	95 ± 5
Baseline medications (prior to study)		
Aldosterone receptor antagonist, n (%)	7 (26)	8 (27)
ACEI or ARB, n (%)	7 (26)	9 (30)
Thiazide diuretic, n (%)	4 (15)	11 (37)
Loop diuretic, n (%)	24 (89)	25 (83)
Study medications		
Bumetanide dose (mg)	3.0 ± 1.4	4.1 ± 3.0
Loop diuretic dose (mg of furosemide equivalents)	120 (IQR 80-160)	160 (IQR 80-220)
Diuretic Efficiency		
Diuretic efficiency (mmmol Na per doubling of loop diuretic dose)	23 (IQR 14-53)	19 (IQR 11-33)

Supplemental Figure 1: Consort diagrams for treatment allocation and missing values for the outpatient (**A**) and inpatient (**B**) cohorts, respectively.

A.

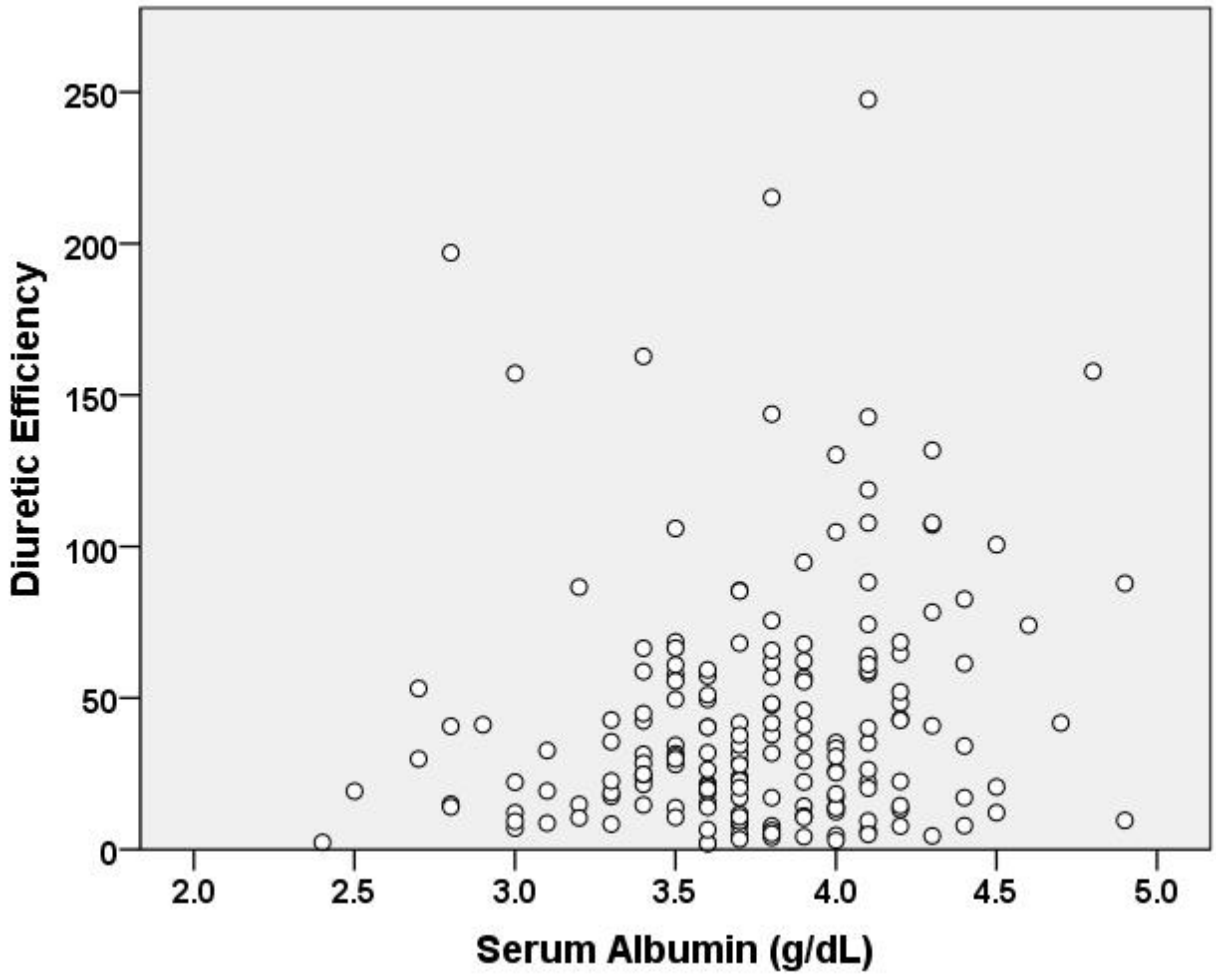


B.

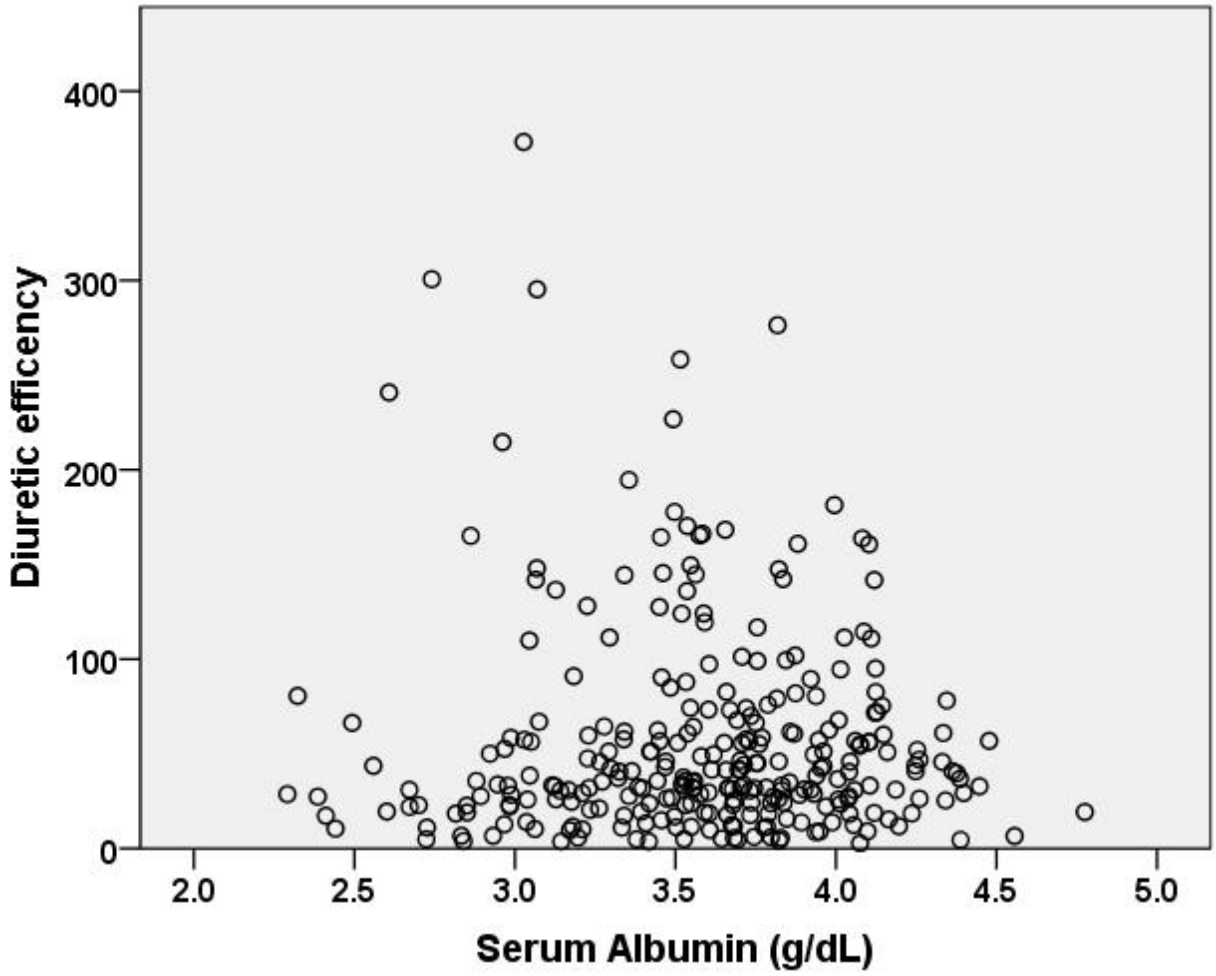


Supplemental Figure 2

A) Scatterplot of the relationship between serum albumin and diuretic efficiency in the outpatient cohort. Diuretic efficiency is expressed in mmol Na per doubling of loop diuretic dose.



B) Scatterplot of the relationship between serum albumin and diuretic efficiency in a second inpatient cohort (see below for details of the cohort). Diuretic efficiency is expressed in mmol of sodium per doubling of loop diuretic dose. Overall correlation between albumin and diuretic efficiency was r=0.06, p=0.32.



Supplemental Methods Section: Patients receiving IV diuretics at Yale New Haven Hospital were considered for enrollment, which could occur at any time during hospitalization (median 1.0 days from admission). Eligibility required a diagnosis of heart failure and a plan by the treating physician for diuresis with intravenous loop diuretics. Exclusion criteria were known bladder dysfunction, incontinence, or inability to comply with timed urine. The data (n=288) comes from the visit day prior to randomization where patients were administered IV loop diuretics at a dose chosen by the provider. Methodology of urine collection was similar to the other inpatient cohort described in the manuscript: Briefly, Prior to receiving IV loop diuretic, all patients were asked to completely empty their bladders. Following administration, there was a timed 6-hour urine collection closely supervised by study staff. The cumulative urine produced was collected and the collection was terminated with a forced void at six hours. All patients provided written informed consent and the study was approved by the Yale Institutional Review Board. Additional details on this cohort are available on clinical.trials.gov (Diagnosing and Targeting Mechanisms of Diuretic Resistance in Heart Failure; NCT02546583).