

Significance of Serum Sodium Concentration in the Very Early Treatment Phase of Congestive Heart Failure Complicated by Advanced Chronic Kidney Disease: Posthoc Analysis of the K-STAR Study

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1. Introduction

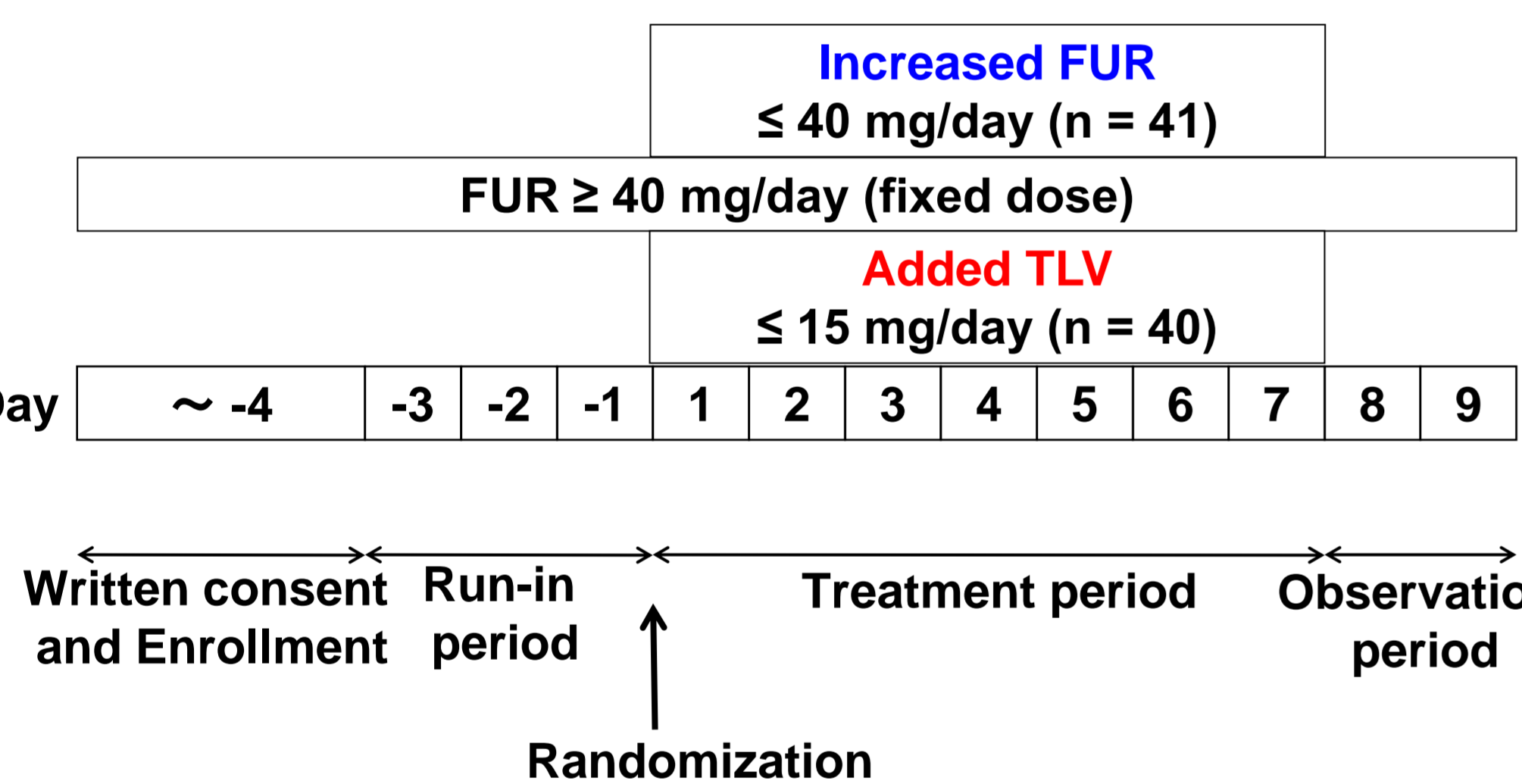
● Although hyponatremia (HypoNa) on admission is a predictor of poor prognosis in acute heart failure (HF) patients, little is known about the association between changes in serum sodium level (sNa) in those with CKD.

● The aim of this posthoc analysis from the K-STAR study was to investigate the clinical significance of pre-existing HypoNa in patients with congestive HF (CHF) complicated by advanced CKD (eGFR < 45 mL/min/1.73m²) in the very early treatment phase.

K-STAR Study

● The K-STAR was a multicenter, open-labeled, randomized, and controlled prospective clinical study consisting of 81 Japanese patients with CHF and residual signs of congestion despite oral furosemide (FUR) treatment (≥ 40 mg/day).

● They were randomly assigned to 7-day treatment with either ≤ 15 mg/day of newly added tolvaptan (TLV) or ≤ 40 mg/day of increased FUR.



2. Patients and Methods

● The posthoc analysis was conducted for 73 patients, except those for whom some results were not available within 2 days from baseline.

● We classified these patients into two groups according to their baseline sNa: HypoNa (sNa ≤ 135 mEq/L, n = 15) and non-HypoNa (sNa > 135 mEq/L, n = 58), and compared various parameters between the groups at baseline (day 1).

● Subsequently, each group was stratified into two subgroups (increased FUR/added TLV), and the differences (Δ) of urine and serum parameters, and physical findings between day 1 and 3 (48 hours), were compared between the subgroups in each group.

● Statistical significance was defined as P < 0.05 (* < 0.05, ** < 0.01 and † < 0.001 in the figures).

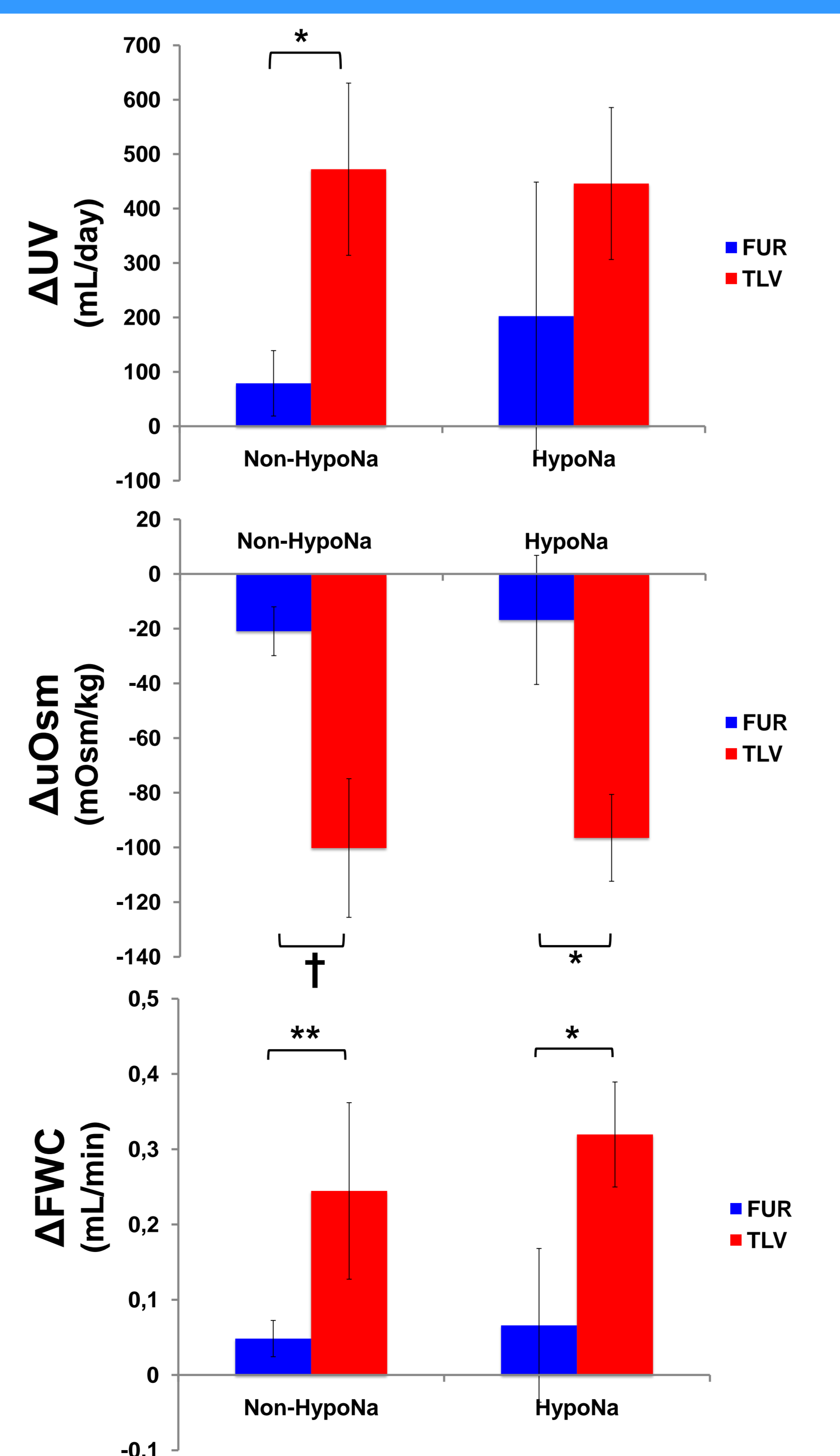
3. Baseline Characteristics

Variables	Total (n = 73)	Non-HypoNa (n = 58)	HypoNa (n = 15)	P value
Demographics				
Age, yrs	75.0 ± 9.6	75.6 ± 10.2	72.7 ± 7.1	0.122
Gender (% male)	60.3	55.2	80.0	0.080
Measurements				
Systolic BP, mmHg	114.2 ± 22.1	117.1 ± 23.0	102.6 ± 13.6	0.023
Weight, kg	60.5 ± 16.2	60.1 ± 17.3	62.2 ± 11.5	0.241
Urine volume, mL/d	1280.0 ± 520.0	1265.7 ± 524.7	1335.0 ± 515.8	0.529
Water intake, mL/d	750.3 ± 329.6	708.3 ± 309.1	910.0 ± 366.5	0.058
UCG and CXR				
LVEF, %	44.9 ± 15.7	45.3 ± 14.3	43.1 ± 20.7	0.503
Lung congestion (% patient)	75.3	74.1	80.0	0.023
Laboratory				
BUN, mg/dL	36.9 ± 16.6	36.5 ± 17.4	38.4 ± 13.3	0.390
sCr, mg/dL	1.9 ± 1.1	2.0 ± 1.2	1.9 ± 0.8	0.769
eGFR, mL/min/1.73m ²	29.7 ± 10.6	29.2 ± 10.5	31.6 ± 10.9	0.449
sNa, mEq/L	138.4 ± 4.3	140.0 ± 2.6	132.4 ± 4.1	<0.001
BNP, pg/mL	608.7 ± 561.8	592.7 ± 516.3	672.5 ± 736.3	0.714
PRA, ng/mL/h	7.4 ± 9.7	4.6 ± 4.4	18.5 ± 15.6	<0.001
sOsm, mOsm/KgH ₂ O	292.8 ± 10.5	295.4 ± 8.9	282.1 ± 9.8	<0.001
uOsm, mOsm/KgH ₂ O	360.3 ± 87.1	365.2 ± 81.3	341.3 ± 108.4	0.293
Free water clearance, mL/min	-0.2 ± 0.2	-0.2 ± 0.2	-0.2 ± 0.3	0.939
FEurea, %	34.8 ± 8.5	35.7 ± 8.8	31.4 ± 6.2	0.095

4. Protocol Treatments

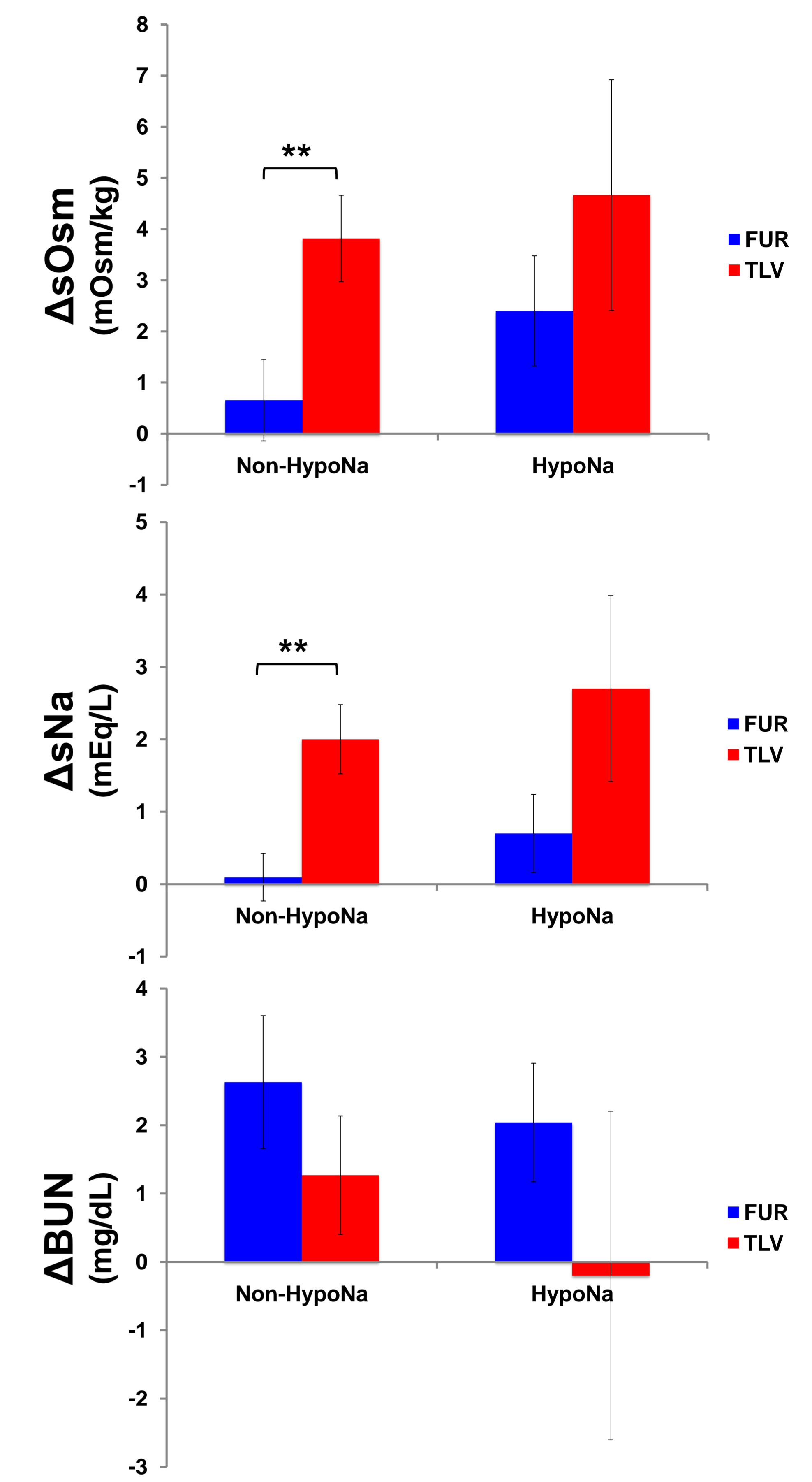
Variables	Non-HypoNa		P value	HypoNa		P value
	FUR (n=32)	TLV (n=26)		FUR (n=5)	TLV (n=10)	
Treatment before admission						
FUR, mg/d	48.1 ± 22.6	55.8 ± 30.7	0.349	56.0 ± 21.9	54.0 ± 23.2	0.825
Treatment after admission						
Increased FUR, mg/d (n = 37)						
Increased FUR, mg/d	26.9 ± 11.5	-	-	32.0 ± 11.0	-	-
Added TLV, mg/d (n = 36)						
Added TLV, mg/d	-	8.1 ± 2.7	-	-	8.6 ± 3.6	-
Total FUR, mg/d (n = 73)	75.0 ± 28.5	55.8 ± 30.7	<0.001	88.0 ± 30.3	54.0 ± 23.2	0.027

5. Results: Urine



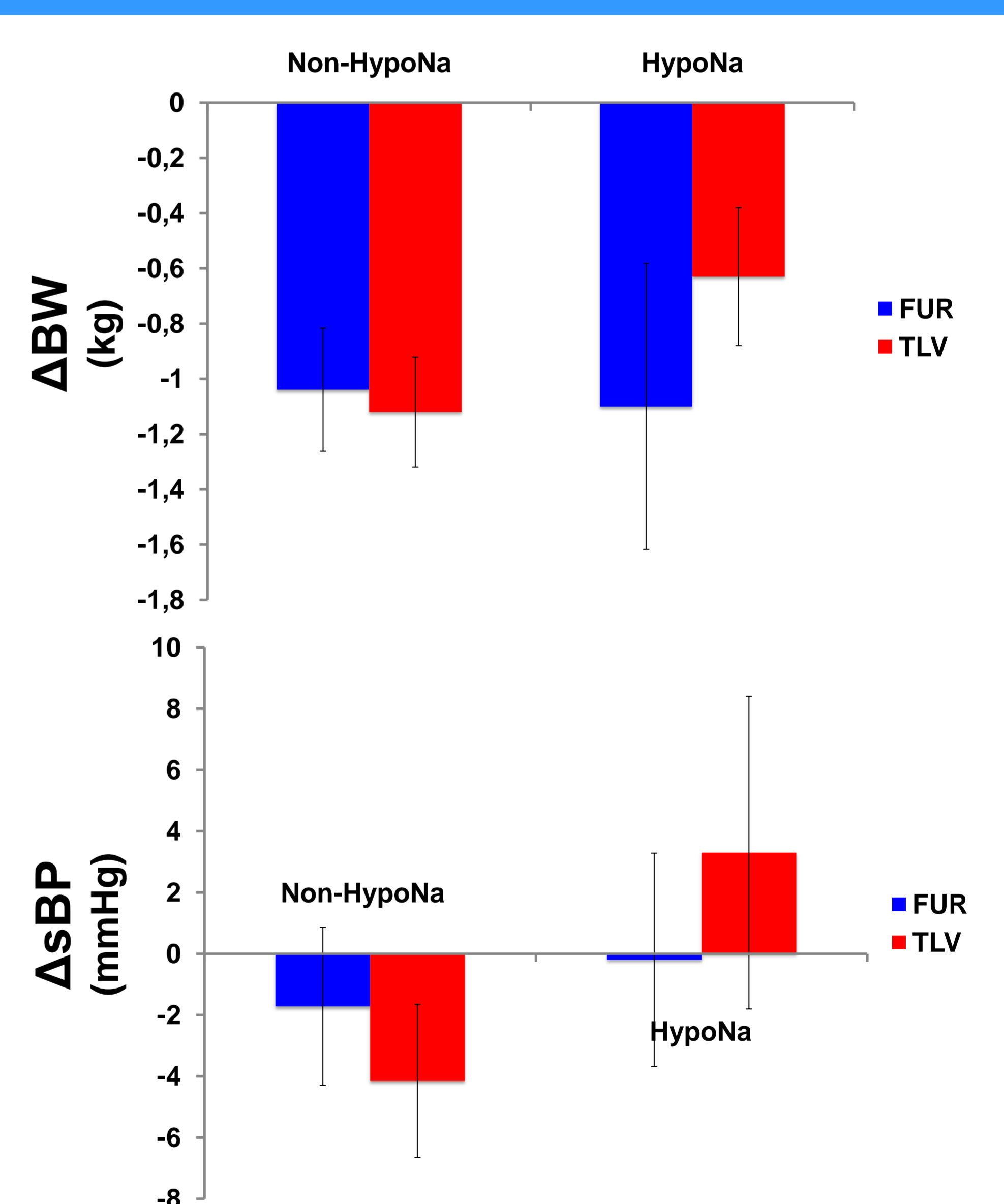
● ΔUV was significantly greater in TLV subgroup than FUR subgroup in non-HypoNa group.
 ● ΔuOsm and ΔFWC were significantly greater in TLV subgroups in both groups.

6. Results: Serum



● ΔsOsm and ΔsNa was significantly greater in TLV subgroup than FUR subgroup in non-HypoNa group.
 ● ΔBUN were lower in TLV subgroups in both groups.

7. Results: BW and BP



● ΔBW and ΔsBP were not significantly different between subgroups in each group.

8. Conclusions

Without significantly affecting either BP or BUN, add-on TLV increased FWC and improved sNa more than increased FUR in CHF patients with advanced CKD, with or without HypoNa.

