

THE EFFECTS OF TOLVAPTON ON SEVERE CHRONIC KIDNEY DISEASE PATIENTS WITH CONGESTIVE HEART FAILURE.



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INTRODUCTION AND AIMS

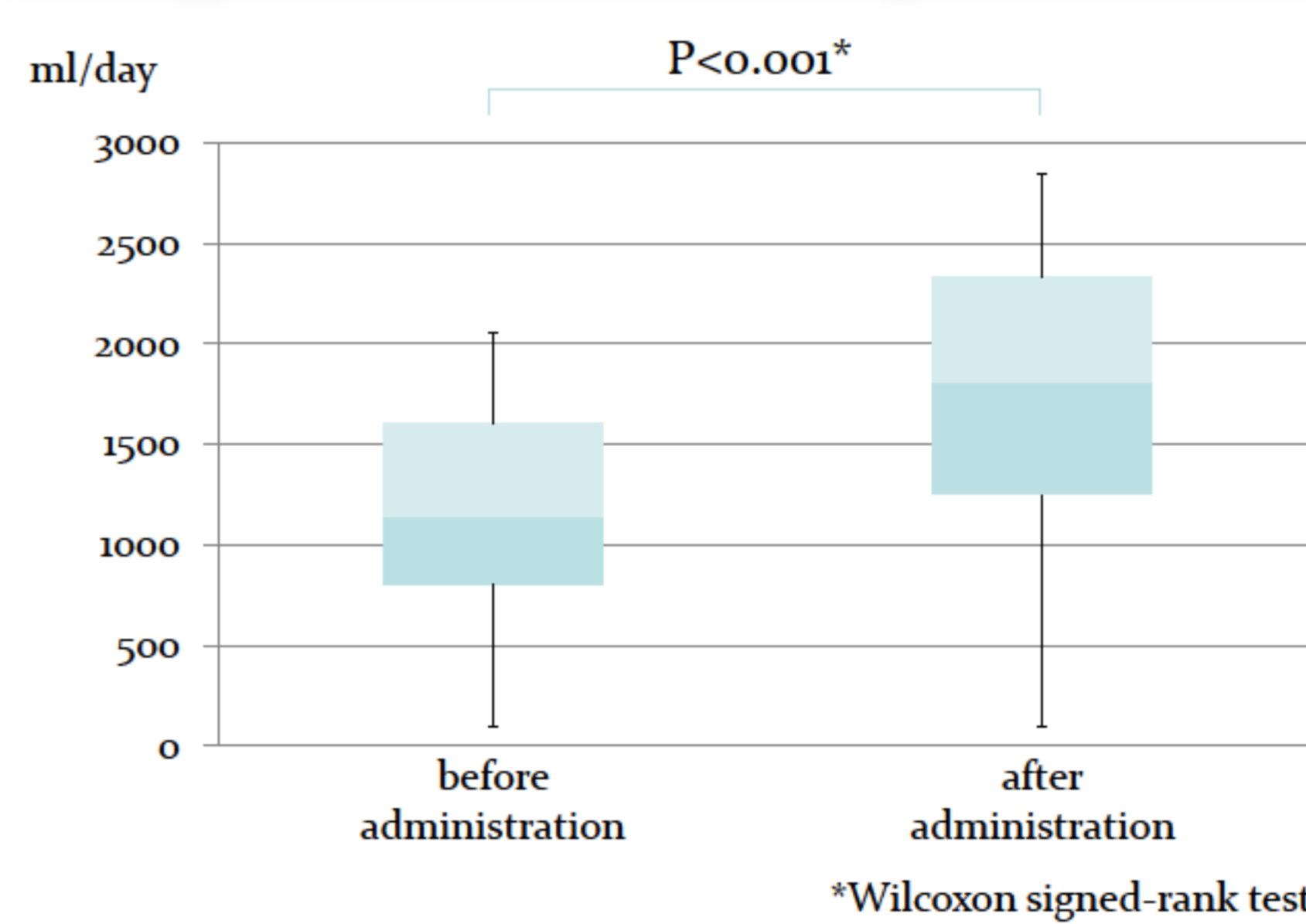
Tolvaptan is a selective vasopressin receptor 2 antagonist and dose-dependent drug used to treat congestive heart failure (CHF) as diuretic. It is known that tolvaptan increases excretion of excess fluids and improves blood sodium levels in patients with heart failure without affecting renal function compared to conventional diuretics. However, few studies examined the effects of tolvaptan for patients with severe chronic kidney disease (CKD). The aim of the study is to examine the effect of tolvaptan on severe CKD patients.

Characteristics	Total(n=75)
Age(years) ,M±SD	75.2±13.3
Gender(male%)	56.0
Diabetes mellitus(%)	41.2
Mean arterial pressure (mmHg) ,M±SD	85.1±20.8
Urine volume (ml/day) ,M±SD	1141.1±539.5
Body weight(kg) ,M±SD	59.7 ± 17.6
eGFR(ml/min/1.73m ²) ,M±SD	17.8±7.4
Serum sodium(mEq/l) ,M±SD	132 ± 6.3
Hemoglobin(g/dl) ,M±SD	10.2±3.6
Albumin(g/dl) ,M±SD	3.0±0.7
Bicarbonate(mEq/l) ,M±SD	19.4±5.5
Brain natriuretic peptide(pg/ml) ,M±SD	2525.5±1421.2
Left Ventricular Ejection Fraction (%) ,M±SD	41.5±16.8
Doses of Tolvaptan(mg) ,M±SD	12.0±5.8

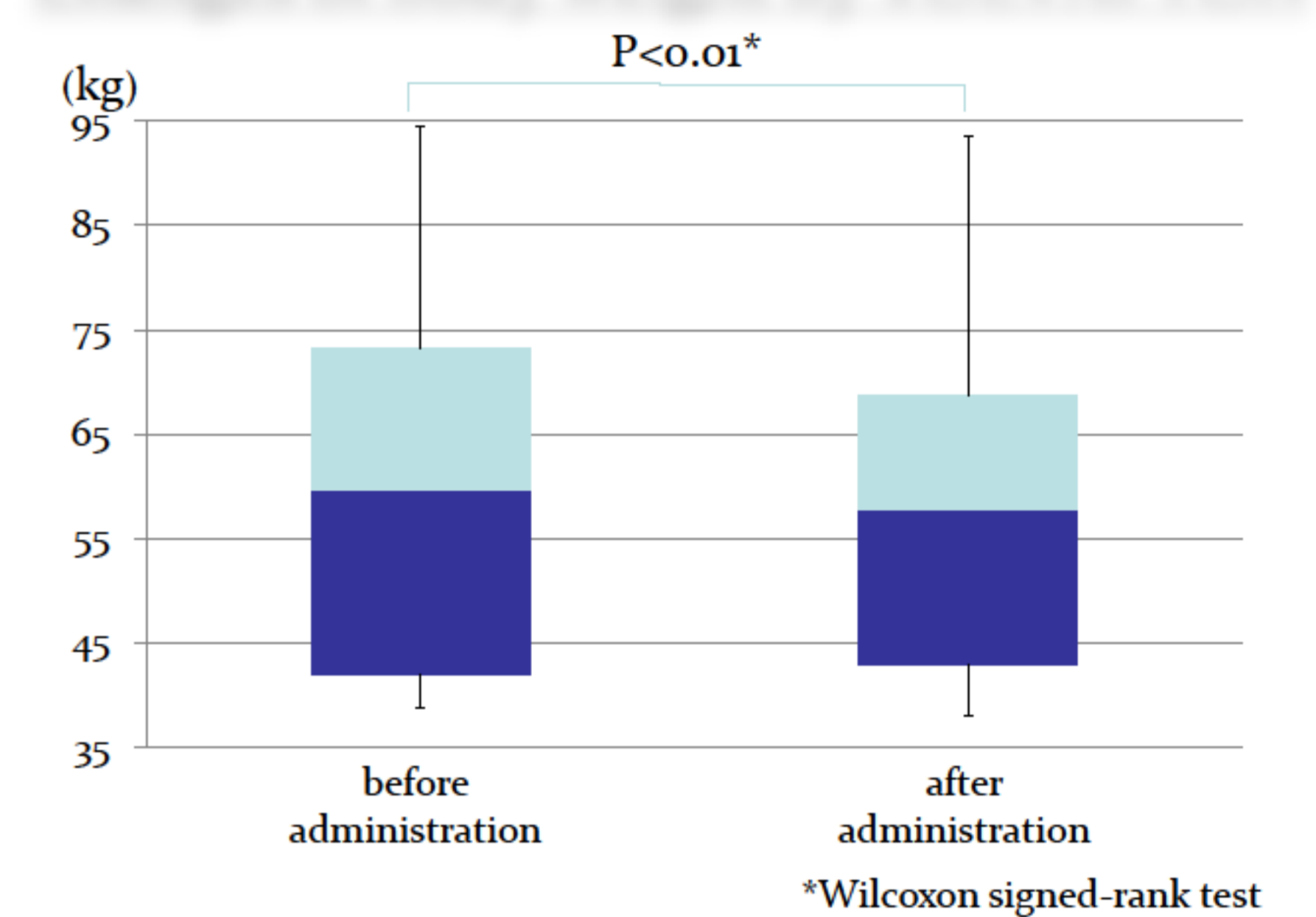
METHODS

We administered tolvaptan (Doses 12.0±5.8 mg) for 75 non-dialysis CKD patients with less than 30 of estimated glomerular filtration rate (male/female: 42/33, 75.2±13.3 years old) in admission. Those of all patients have already treated conventional diuretics. The patients who changed the dose of conventional diuretics in observation period were excluded. To evaluate the effect of tolvaptan, the following data were collected from the electric record for three days after administration: age, sex, presence of diabetes, blood pressure, urine volume, body weight, estimated glomerular filtration rate (eGFR), serum sodium concentration, hemoglobin, serum albumin, serum bicarbonate, brain natriuretic peptide (BNP), and cardiac ejection fraction. We defined 20% increase of urine output from baseline after administration of tolvaptan as responder and statistical analysis was used by logistic regression models.

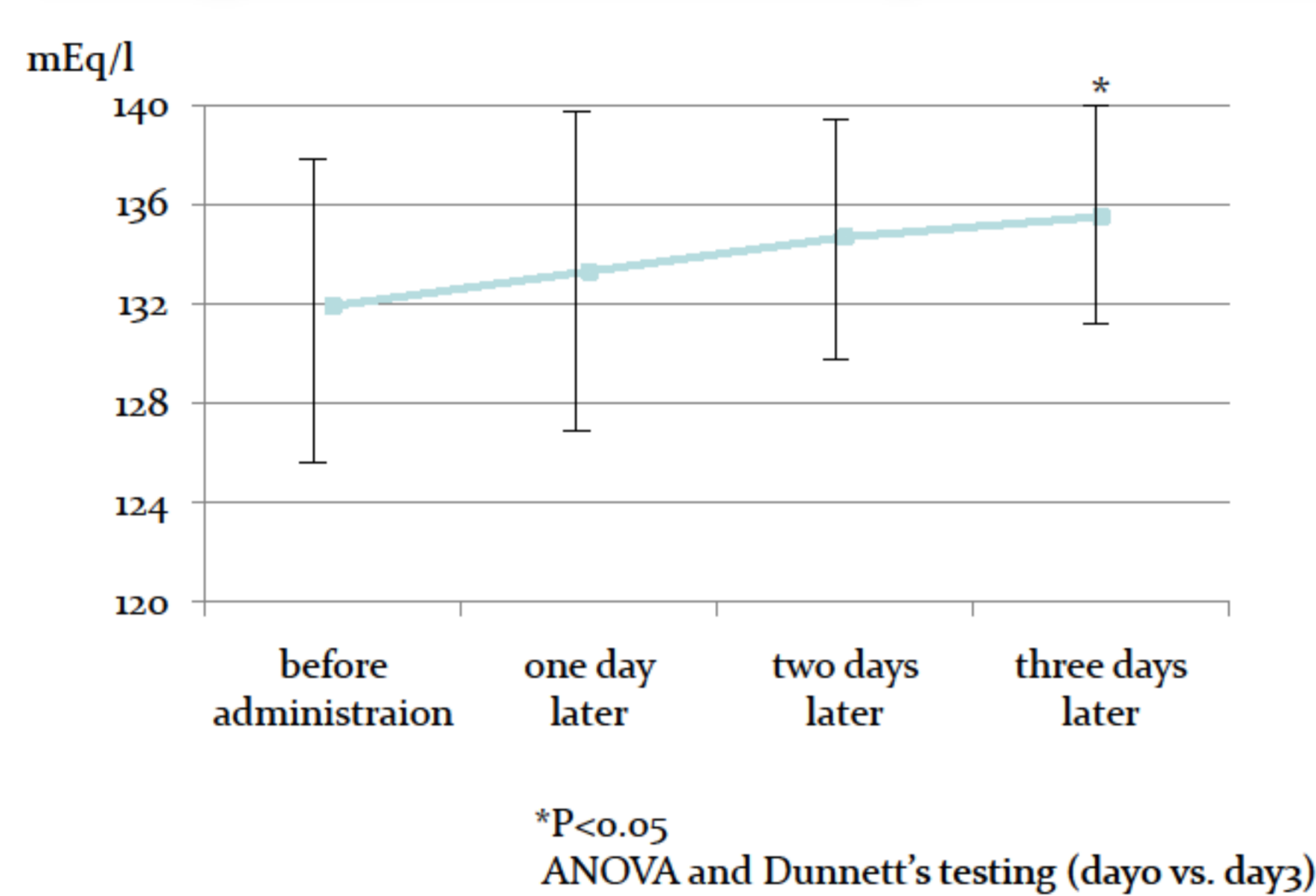
Changes of Urine volume by TOLVAPTON



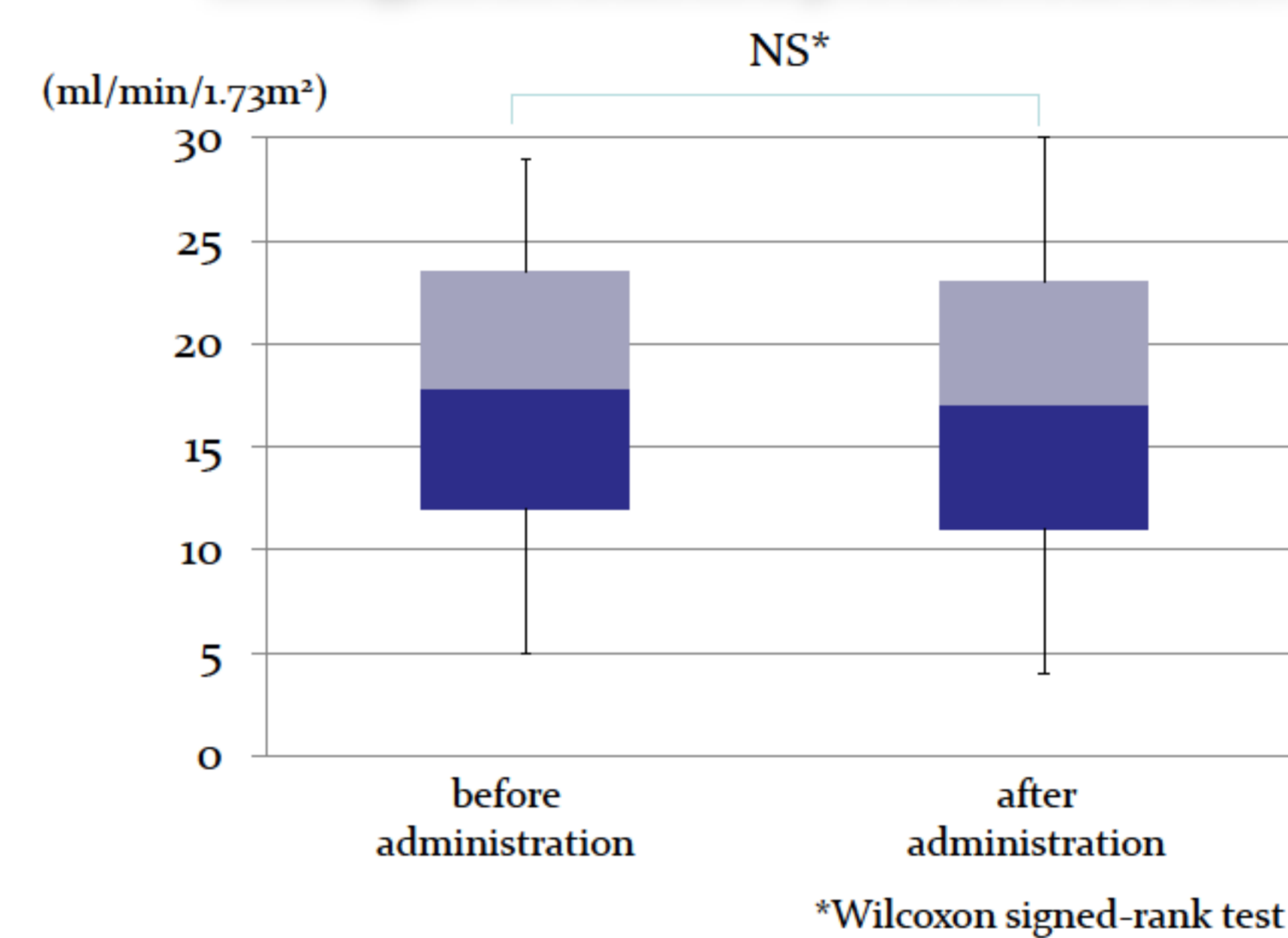
Changes of Body weight by TOLVAPTON



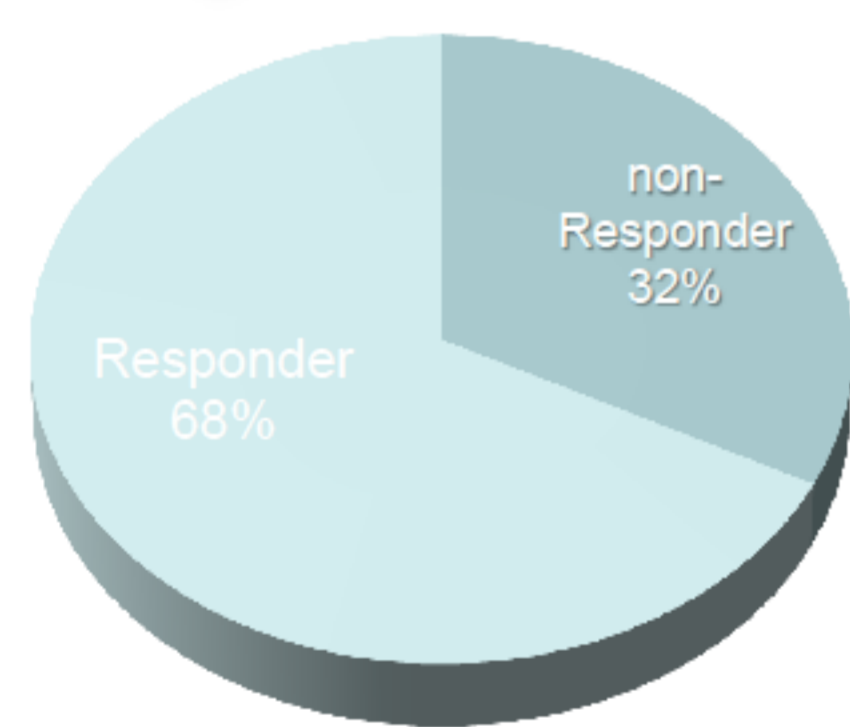
Changes of serum sodium by TOLVAPTON



Changes of eGFR by TOLVAPTON



The ratio of Responder and non-Responder



Responder:
The patients of 20% increase of urine output from baseline after administration of tolvaptan

Univariate analysis

	Odds ratio	95%CI	P value
age	1.008	0.94-1.08	0.78
Sex (male/female)	0.68	0.17-2.60	0.57
eGFR	1.43	1.11-1.65	0.003*
Cardiac ejection fraction	1.18	1.11-1.34	0.008*
Diabetes mellitus	0.27	0.053-1.14	0.09
Urine volume (oliguria/non-oliguria)	1.87	1.45-2.13	0.0016*
Hemoglobin	1.004	0.97-1.02	0.69
Mean Arterial Pressure	1.006	0.97-1.04	0.67

(Logistic regression model)

Multivariate analysis

	Odds ratio	95%CI	P value
age	1.009	0.90-1.11	0.98
Sex (male/female)	0.49	0.04-2.93	0.37
eGFR	1.30	1.19-1.45	0.02*
Cardiac ejection fraction	1.18	0.95-1.33	0.11
Urine volume (oliguria/non-oliguria)	1.67	1.36-1.99	0.004*

(Logistic regression model)

RESULTS

Tolvaptan increased urinary volume from 1141.1±539.5 ml/day to 1864.5±1008.2 ml/day ($p < 0.001$, Wilcoxon signed-rank test), improved Body weight from 59.7 ± 17.6 kg to 57.8 ± 17.0 kg ($p < 0.01$, Wilcoxon signed-rank test), and elevated serum sodium from 132 ± 6.3 mEq/l to 139.4 ± 6.4 mEq/l ($p = 0.03$, ANOVA and Dunnett's testing). eGFR (17.8±7.4 at baseline) remained 17.1±8.7 after administration ($p = 0.34$, Wilcoxon signed-rank test).

In univariate analysis, eGFR (Odds ratio 1.43, 95%CI 1.11-1.65, $p = 0.003$), urine volume at baseline (1.87, 1.45-2.14, $p < 0.001$), and cardiac ejection fraction (1.18, 1.11-1.34, $p = 0.008$) were associated with responder.

In multivariate analysis, eGFR (Odds ratio 1.30, 95%CI 1.19-1.45, $p = 0.02$), urine volume at baseline (1.67, 1.36-1.99, $p = 0.004$) were remained significant after adjusted for age, sex, eGFR, serum albumin, urine volume, and cardiac ejection fraction.

CONCLUSIONS

Tolvaptan is effective diuretic even with severe CKD patients, resistance to conventional diuretics, without worsening renal function, but the effectiveness decreases for the patients with lower eGFR and urine volume at baseline.

REFERENCES:

*Otsuka et al: The effects of tolvaptan on patients with severe chronic kidney disease complicated by congestive heart failure. Clin Exp Nephrol. 2013 Mar 13. [Epub ahead of print]

