The Role of Brain Natriuretic Peptide for Prediction of Renal Outcome and Fluid Management in the Critically Ill Patients

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Objectives:

Fluid overload is associated with acute kidney injury (AKI) and mortality. There is no convenient, precise method to guide fluid therapy of critically ill patients. We aimed to investigate whether brain natriuretic peptide (BNP) can predict renal outcome and mortality of critically ill patients as well as be the potential guidance for the fluid management.

Methods:

This prospective observational study included patients who were admitted to the intensive care unit (ICU). Patients with underlying heart disease and heart dysfunction were excluded. Plasma BNP levels were obtained on admission (D0), 24 (D1) and 48 hours (D2) later. The primary outcome was AKI development during ICU duration and recovery of AKI at ICU discharge, and the secondary outcome was in-ICU mortality.

Results:

163 patients were enrolled for analysis. Delta-BNP level within initial 24 hours after ICU admission significantly correlated with delta-central venous pressure levels ($r = 0.219$, $p = 0.010$) rather than fluid accumulation. Delta-BNP levels within initial 24 hours of less than 81.8% was an independent predictor of better renal outcome (no-AKI or AKI with recovery). Besides, the increment in the BNP level from D0 to D1 was a significant risk factor of mortality. In priori subgroup analysis for patients with sepsis, delta-BNP levels from D0 to D1 remained a significant predictor of renal outcome and mortality.

Table 1

Variable	All (n = 163)	AKI without recovery (n =26)	No-AKI or AKI with recovery (n = 99)	P value
Demographics				
Age (years)	67.5 (±13.4)	71.4 (±12.0)	67.0 (±13.5)	0.21
Male (%)	106 (65.0)	16 (61.5)	90 (65.7)	0.68
Baseline creatinine (mg/dl)	1.04 (±0.68)	1.27 (±1.02)	1.01 (±0.61)	0.12
Comorbid disease				
Diabetes mellitus (%)	68 (41.7)	9 (34.6)	59 (43.1)	0.42
Hypertension (%)	83 (50.9)	14 (53.8)	70 (51.1)	0.85
CKD (%)	29 (11.7)	3 (11.5)	16 (11.7)	0.98
Pulmonary disease (%)	22 (13.5)	5 (19.3)	17 (12.4)	0.35
Liver cirrhosis (%)	20 (12.3)	3 (11.5)	17 (12.4)	0.90
Malignancy (%)	11 (6.7)	5 (19.2)	6 (4.4)	< 0.01
CVA (%)	14 (8.6)	2 (7.7)	12 (8.7)	0.86
Clinical parameters on ICU admission				
Mean arterial pressure (mmHg)	81.1 (±19.3)	88.2 (±21.8)	80.0 (±18.5)	0.17
Temperature (°C)	36.4 (±1.5)	36.5 (±1.4)	36.4 (±1.6)	0.71
Heart rate	107.2 (±21.4)	117.3 (±19.7)	105.8 (±21.6)	0.02
Serum creatinine (mg/dl)	2.3 (±2.0)	3.3 (±2.6)	2.2 (±1.8)	0.02
Hemoglobin (g/dl)	11.1 (±2.5)	10.7 (±2.5)	11.2 (±2.5)	0.40
WBC (/µL)	14786.0 (±9323.8)	10709.5 (±9247.2)	15854.1 (±9227.0)	0.05
Serum sodium (mmol/L)	184.6 (±8.4)	135.5 (±10.4)	184.5 (±8.2)	0.73
Serum potassium (mmol/L)	4.0 (±0.9)	4.0 (±0.7)	4.0 (±0.9)	0.90
Serum lactate (mmol/L)	1.1 (±0.8)	1.4 (±0.6)	1.1 (±0.8)	0.01
Serum albumin (g/dl)	3.0 (±0.6)	3.0 (±0.6)	3.0 (±0.6)	0.73
BNP D0 (pg/ml)	749.9 (±919.9)	968.6 (±899.4)	719.8 (±955.2)	0.26
BW D0 (Kg)	57.8 (±13.3)	60.6 (±13.8)	57.4 (±13.2)	0.17
CVP level	10.3 (±6.1)	10.7 (±4.6)	10.2 (±6.3)	0.76
APACHE II score	21.2 (±8.6)	27.4 (±7.2)	20.3 (±8.3)	< 0.01
SOFA score	8.0 (±3.5)	9.5 (±2.7)	7.7 (±3.5)	< 0.01
GCS score	11.6 (±3.6)	11.3 (±2.9)	11.6 (±2.9)	0.60
ICU course				
Peaked serum creatinine of AKI (mg/dl)		3.3 (±2.5)	2.6 (±1.8)	0.09
Serum creatinine on ICU discharge (mg/dl)		4.6 (±0.7)	1.5 (±1.8)	< 0.01
BNP D1 (pg/ml)	1033.9 (±1802.0)	2324.4 (±4303.9)	852.3 (±979.8)	0.01
BNP D2 (pg/ml)	973.4 (±1304.2)	2004.4 (±4131.7)	828.3 (±1113.8)	0.01
BW D1 (Kg)	59.0 (±13.8)	62.3 (±13.9)	58.5 (±12.9)	0.24
BW D2 (Kg)	59.7 (±12.8)	62.9 (±14.3)	59.1 (±12.4)	0.24
Fluid accumulation D1 (ml)	2046.0 (±2718.2)	2964.7 (±2589.0)	1916.7 (±2760.8)	0.12
Fluid accumulation D2 (ml)	2132.1 (±3291.4)	3254.9 (±3210.3)	1974.1 (±3283.6)	0.07
Fluid accumulation during ICU stay (ml)	1934.6 (±4733.5)	4433.4 (±4231.7)	1583.0 (±4708.3)	0.01
Sepsis (%)	119 (73.0)	19 (73.0)	100 (73.0)	0.25
Use of inotropic or vasopressor drugs (%)	112 (68.1)	17 (65.4)	94 (68.6)	0.60
Dialysis (%)	25 (15.3)	8 (30.8)	17 (12.4)	< 0.01
Mechanical ventilation (%)	76 (16.0)	8 (30.8)	18 (13.1)	0.04
ICU mortality (%)	42 (25.8)	13 (50.0)	39 (21.3)	< 0.01
ICU stay (day)	7.3 (±6.9)	10.1 (±12.6)	6.9 (±5.7)	0.01

TABLE 2. Multivariate analysis of the predictors of no-AKI or AKI with recovery by fitting multiple logistic regression models with the stepwise variable selection method

Covariate	Estimated Regression Coefficient	Estimated Standard Error	z Value	p Value	Estimated Odds Ratio	95% Confidence Interval
Intercept	3.952	2.141	1.853	0.065	--	--
Change of BNP D_{01} (%) < 81.8%	2.846	1.148	2.481	0.013	17.21	1.64 – 177.06
8954/µL ≤ WBC < 27663/µL	2.290	0.700	3.272	0.001	9.88	2.74 – 44.53
Hb ≥ 12.2 g/dL	1.877	0.807	2.334	0.020	6.53	1.53 – 37.62
118 mmol/L ≤ Na < 145 mmol/L	1.792	0.904	0.981	0.047	6.00	1.02 – 38.64
Heart rate	- 0.040	0.016	- 2.493	0.013	0.96	0.93 – 0.99
APACHE II score	- 0.118	0.043	- 2.721	0.007	0.89	0.81 – 0.96

TABLE 3. Multivariate analysis of the predictors of no-AKI or AKI with recovery in the subgroup analysis of patients with sepsis

Covariate	Estimated Regression Coefficient	Estimated Standard Error	z Value	p Value	Estimated Odds Ratio	95% Confidence Interval
Intercept	8.222	2.499	3.291	0.001	--	--
Change of BNP D_{01} (%) ≥ 81.8% × Sepsis	- 4.062	1.367	- 2.973	0.003	0.02	<0.01 – 0.25
Fluid accumulation during ICU stay × No sepsis	- 0.002	0.001	- 2.392	0.017	0.99	0.99 – 0.99
8954/µL ≤ WBC < 27663/µL	2.745	0.754	3.641	< 0.001	15.56	3.98 – 79.79
Hb ≥ 12.2 g/dL	2.182	0.866	2.524	0.012	8.87	1.89 – 58.41
118 mmol/L ≤ Na < 145 mmol/L	2.032	0.953	2.132	0.033	7.63	1.22 – 57.02
Heart rate	- 0.051	0.018	- 2.833	0.005	0.95	0.91 – 0.98
APACHE II score	- 0.150	0.047	- 3.151	0.002	0.86	0.78 – 0.94

TABLE 4. Multivariate analysis of the predictors of ICU mortality fitting multiple logistic regression models with the stepwise variable selection method

| Covariate	Estimated Regression Coefficient	Estimated Standard Error	z Value	p Value	Estimated Odds Ratio	95% Confidence Interval
Intercept	- 1.367	1.526	-0.901	0.370	--	--
Malignancy	2.370	1.090	2.172	0.030	10.70	1.31 – 97.02
Age ≥ 58 years old	1.823	0.727	2.511	0.012	6.19	1.64 – 29.21
MBP < 70 mmHg or ≥ 113 mmHg	1.149	0.558	2.064	0.040	3.15	1.07 – 9.77
SOFA score	0.335	0.111	3.032	0.002	1.40	1.14 – 1.77
Serum creatinine on ICU admission (mg/dL)	0.250	0.127	1.963	0.050	1.28	1.00 – 1.70
Change of BNP D_{01}	0.001	0.0003	2.891	0.004	1.01	1.00 – 1.01
Serum albumin (g/dl)	- 1.643	0.464	-3.544	< 0.001	0.19	0.07 – 0.46
Use of inotropic or vasopressor drugs	- 1.779	0.734	- 2.422	0.015	0.17	0.04 – 0.69
Fluid accumulation during ICU stay (mL)	0.001	0.0003	1.821	0.069	1.01	0.99 – 1.01
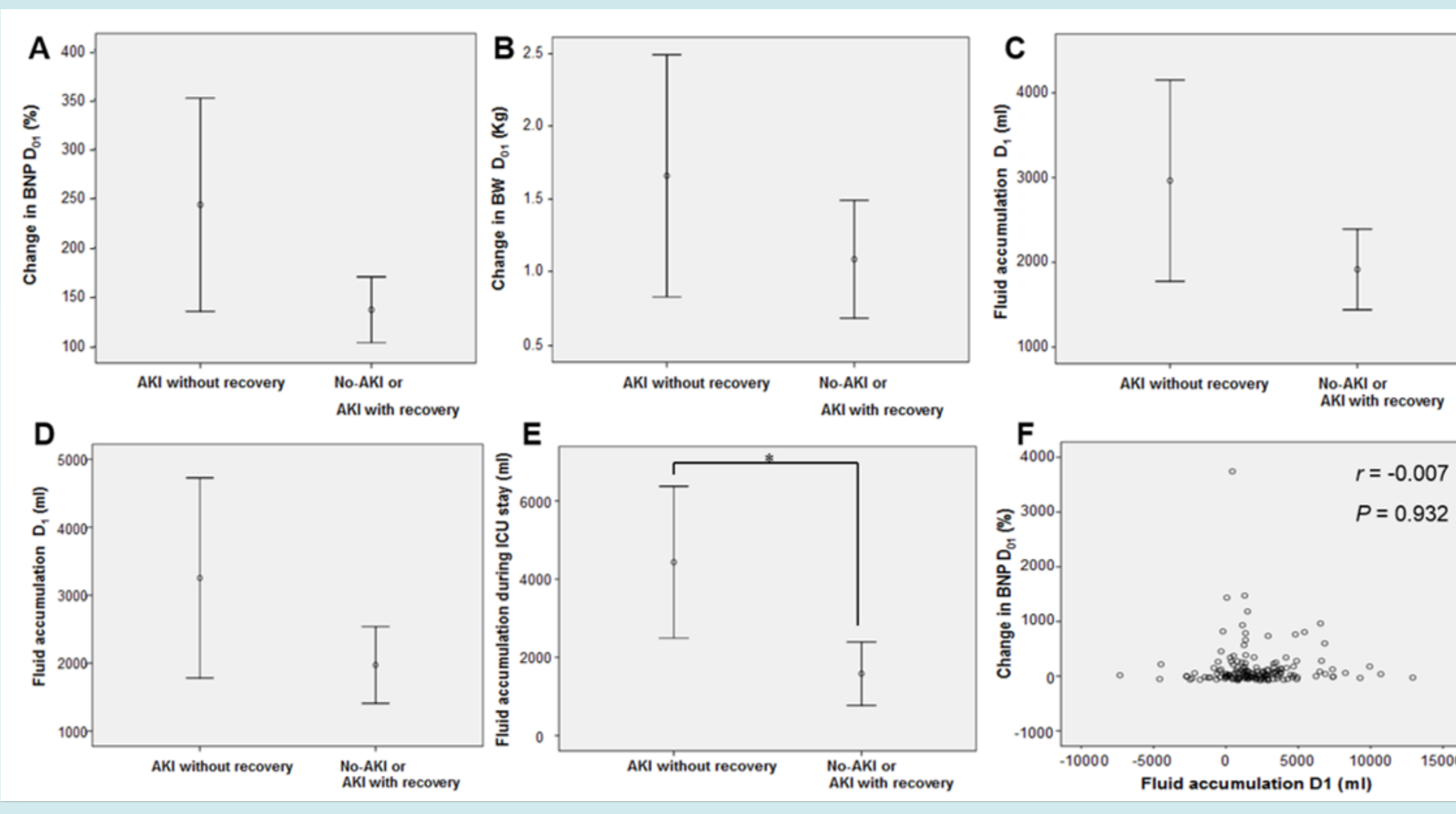
Figure 1 Percent change in BNP level from D0 to D1 (A), change in BW from D0 to D1 (B), fluid accumulation D1 (C), fluid accumulation D2 (D), fluid accumulation during ICU stay (E) between no-AKI or AKI with recovery group and AKI without recovery group. Correlation scatter plot of percent change in BNP level from D0 to D1 and fluid accumulation in D1 (F). BNP = brain natriuretic peptide, BW = body weight, AKI = acute kidney injury, ICU = intensive care unit, D0 = day 0 (on ICU admission), D1 = day 1, D2 = day 2. **$p < 0.01$.
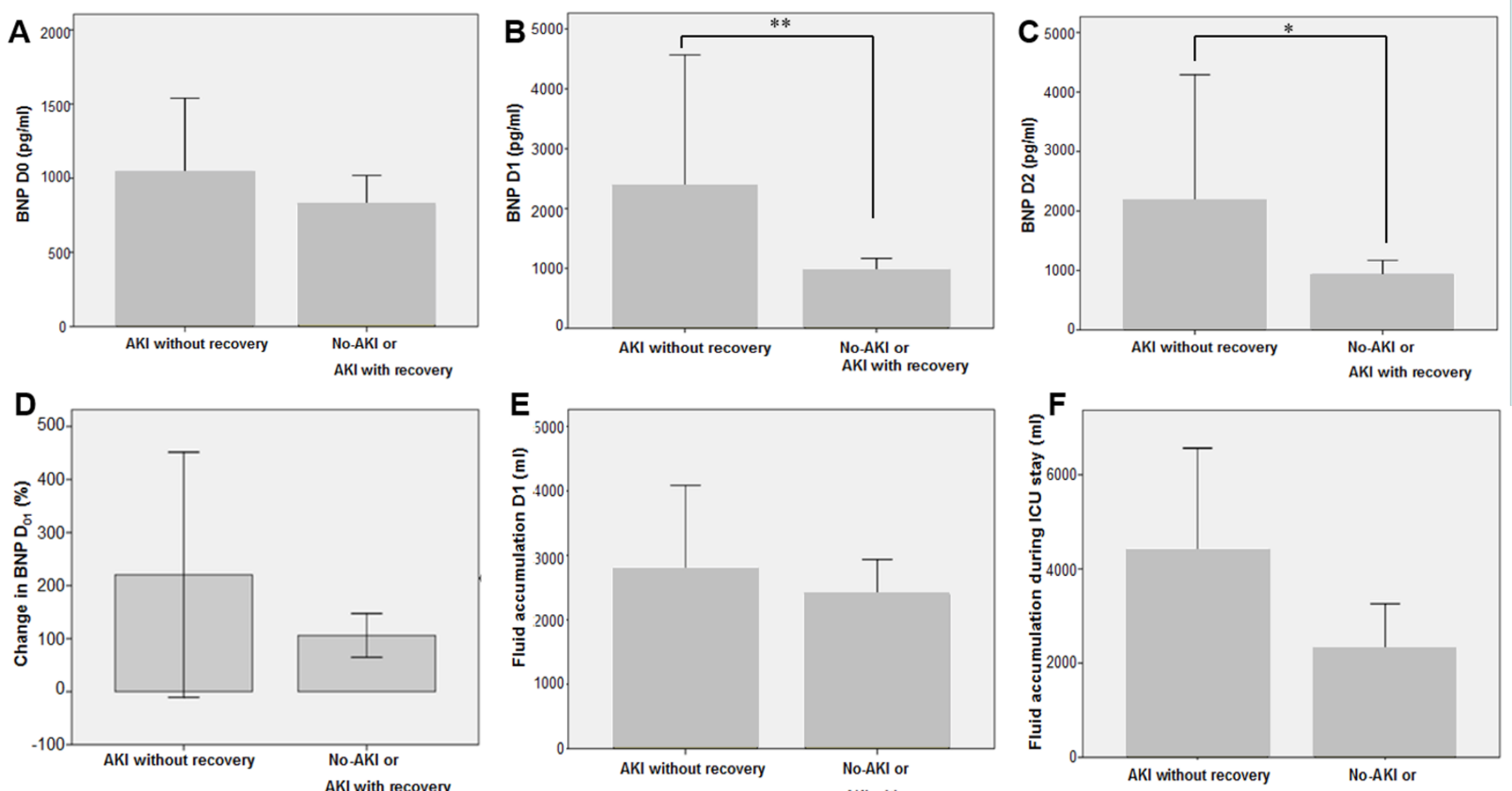
Figure 2 In septic patients, BNP level on D0 (A), BNP level on D1 (B), BNP level on D2 (C), percent change in BNP level from D0 to D1 (D), fluid accumulation on D1 (E), fluid accumulation during entire ICU stay (F) between no-AKI or AKI with recovery group and AKI without recovery group. BNP = brain natriuretic peptide, ICU = intensive care unit, D0 = day 0 (on ICU admission), D1 = day 1, D2 = day 2. * $p < 0.05$, ** $p < 0.01$.
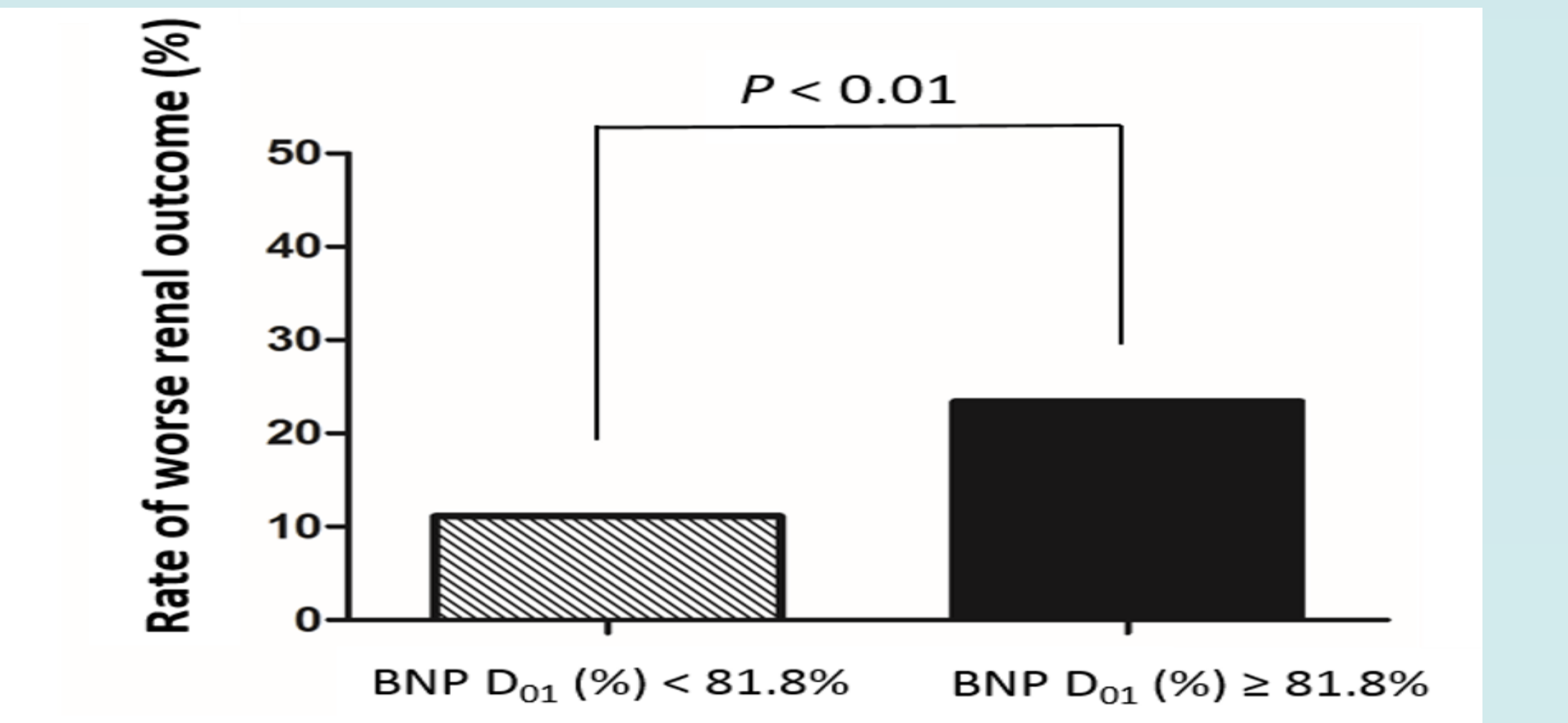
Fig. 3 Patients with change of BNP D_{01} (%) < 81.8% had lower rate of worse renal outcome. BNP D_{01}= change of brain natriuretic peptide from day 0 (on ICU admission) to day 1

Conclusions:

Our study has shown that delta-BNP levels within 24 hours of admission to the ICU are better than fluid accumulation as the predictors of AKI, recovery, and mortality.

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