SALT WATER DISEQUILIBRIUM AND FLUID OVERLOAD IN HEMODYALYSES PATIENTS: A CENTRAL ROLE OF CORIN

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Introduction and Aim

Cardiovascular disease accounts for >50% of deaths in patients with end-stage renal disease (ESRD), representing the major determinant of prognosis.
Natriuretic peptides (NP) plays a role in the management of salt and water balance. The serin-protease Corin, activates NP, and plays an important role in the control of blood pressure and cardiac function. The aim of the study was to identify the role of Corin in renal physiopathology, analyzing its levels in dialyzed patients, and evaluating its relation with fluid overload and comorbidities such as heart failure and blood hypertension.

Methods

Patients and controls
20 adult patients on intermittent hemodialysis (HD) treatment, referred to the Nephrology and Dialysis Unit of Messina University Hospital, were enrolled for the study. Patients with inflammatory disease or a diagnosis of cancer were excluded from the study. The HD sessions, of 3 to 4 hours duration, took place three times a week; the blood flow was more than 250 ml/min, bicarbonate infusion 2000 ml/h, the Acetate Free Biofiltration (AFB) technique being employed, with the Integra (Hospal, Bologna, Italy) monitor. The artero-venous fistula was the vascular access for hemodialysis in all patients. In patients receiving HD, blood samples were collected in the morning at 08.00 h immediately before and just after haemodialysis from the arterial line of the HD, while in a healthy control group blood samples were collected at 08:00 h following an overnight fast.
Blood samples were collected into chilled vacutainer tubes containing potassium ethylenediamine tetracetate. Tubes were instantly cooled on ice and centrifuged at 3000 rpm for 10 min at 4∘C within 30 min. Serum was stored at −80°C until analyzed Corin was measured using a commercial available ELISA kit (R&D Systems, Inc. Minneapolis). Statistical analyses were performed with NCSS for Windows (version 4.0), the MedCalc (version 11.0; MedCalc Software Acacialaan, Ostend, Belgium) Data were presented as mean ± SD for normally distributed values and median [IQ range] for non-normally distributed values. .

Results:

Corin levels were significantly higher in HD patients than in healthy subjects, both in pre-HD (1609.7 ± 757.2 vs 678.7 ± 149.4 pg/ml, p<0.0001) and in post-HD analyses (1568.3 ± 591.7 vs 678.7 ± 149.4 pg/ml, p<0.0001). No significant differences were found between corin levels before and after a single dialytic session (1609.7 ± 757.2 vs 1568.3 ± 591.7 pg/ml; p=0.76). In fact, no trace of corin was revealed in dialysate effluent samples **Figure 1.**
According to comorbidities and corin levels, patients were divided into subgroups. In particular hypertensive patients were characterized by higher corin values than those observed in normotensive subjects (1712.6 ± 727.1 vs 691.6 ± 11.8; p<0.0001). Similarly, heart failure group was characterized by high corin levels if compared to patients with normal heart function (1808.7 ± 714.5 vs 813.4 ± 150.3; p=0.0001).**Figure 2.**
At univariate analysis, corin was found to be directly correlated with dialysis vintage (r=0.80; p<0.0001), parathyroid hormone (PTH) (r=0.60; p=0.006), tricuspid annular plane systolic excursion (TAPSE) (r=0.95; p=0.0002) and presence of heart failure (r=0.53; p=0.01), whereas a significant inverse correlations were evidenced for systolic blood pressure (r= -0.55; p=0.01) and body weight (r= -0.46; p=0.03). In addition, post-dialysis corin values correlate inversely with systolic (r= -0.61; p=0.004) and diastolic (r = -0.63; p=0.0002) blood pressure levels assessed at the end of dialytic treatment. Moreover it inversely correlated with Δ weight (r= - 0.50; p=0.02). These findings are summarized in **Figure 3**.
*Multiple regression analysis*
All variables found to be significantly correlated with Corin at univariate analysis were introduced in a multivariate model using corin as a dependent variable. After adjustment for other factors, significance was maintained for the correlation between corin and dialysis vintage (β=0.83;p=0.0002), heart failure (β =0.42;p<0.0001), systolic blood pressure (β = - 0.70 ; p=0.0002) and body weight (β = - 0.39;p<0.0001). In contrast, the correlations with PTH and TAPSE found at univariate analysis, were lost
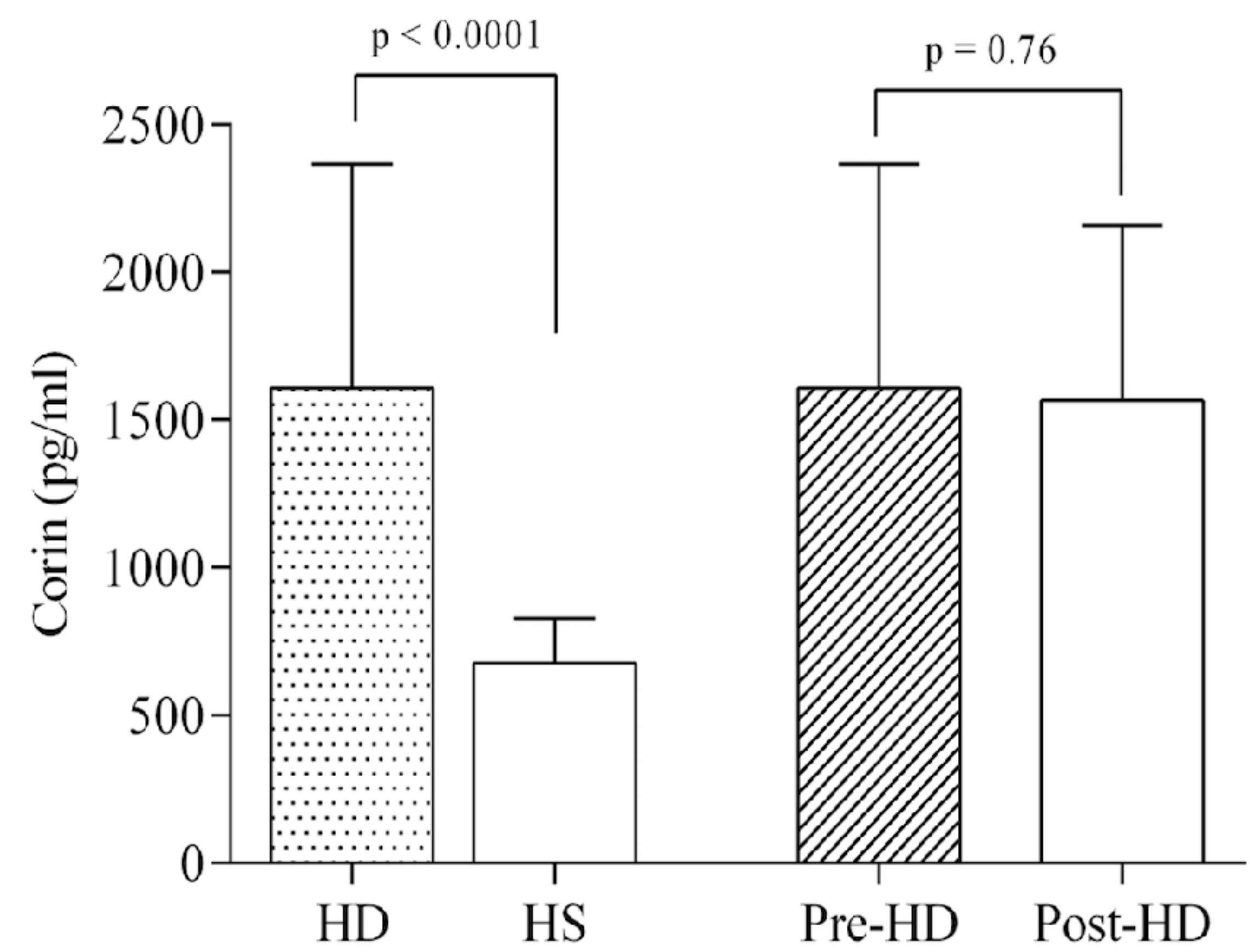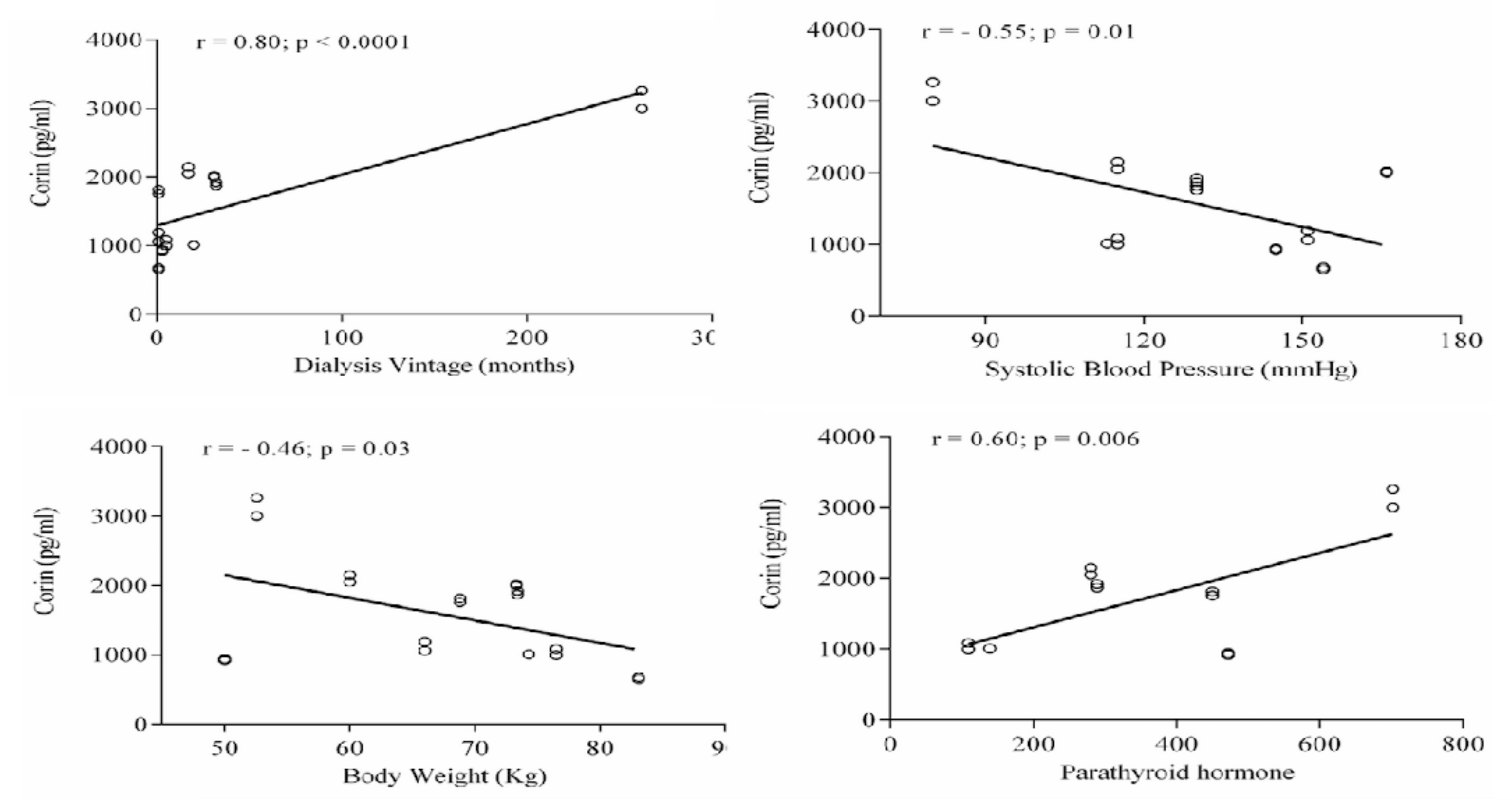

Figure 1: Corin levels in HD patients.
Corin values were significantly higher than in healthy subjects; no significant differences between the levels of corin in uremic patients before and after a single dialysis session
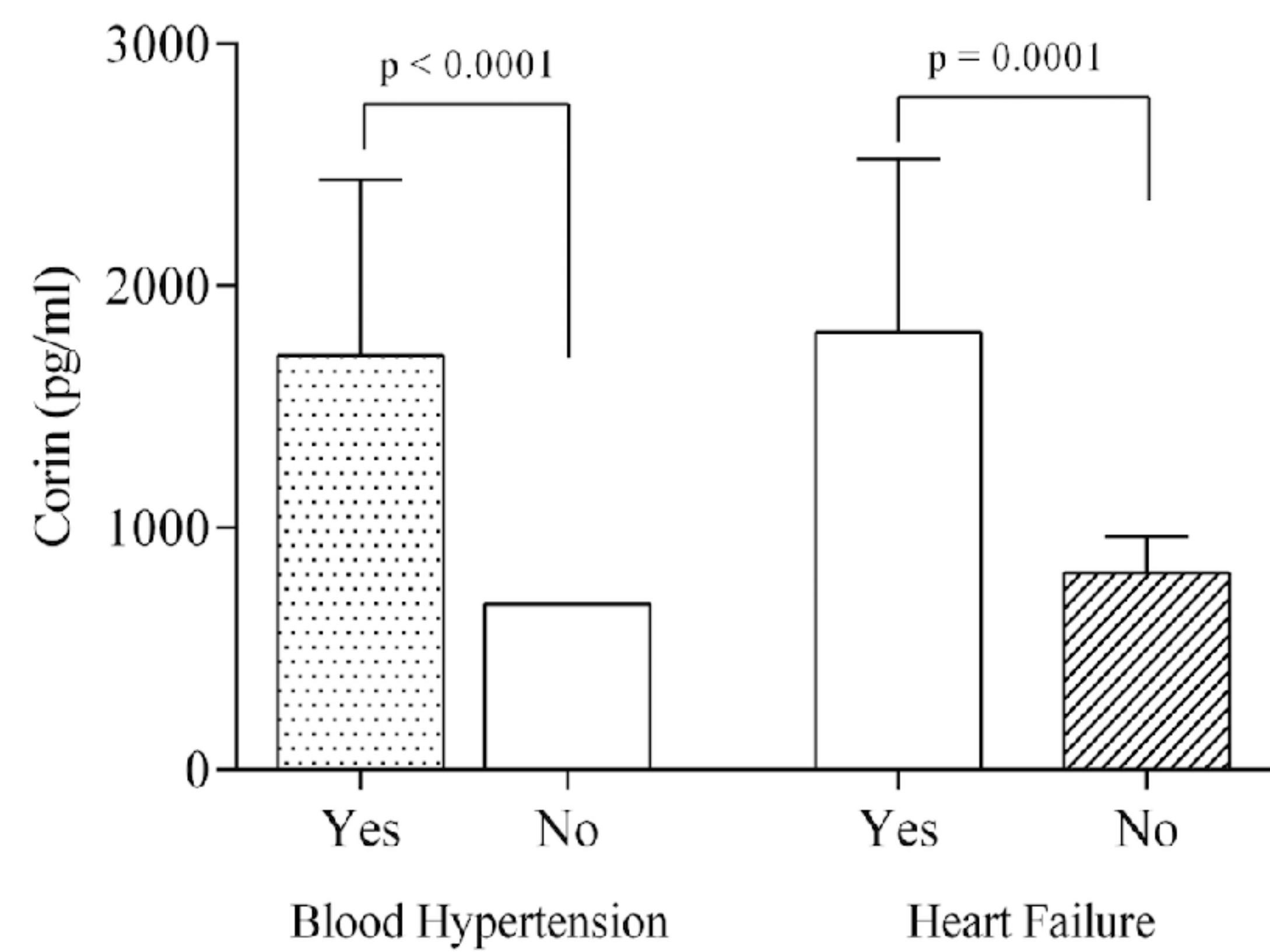
Figure 2: Scatterplot of Corin values in hypertensive or normotensive HD patients and in patient with or without heart failure.

Figure 3: Univariate relationships of Corin in HD patients.

Conclusions

Corin seems to be implicated in the regulation of salt and water balance and the disturbances of volume homeostasis of HD patients. However, further studies are warranted to understand the role of corin in kidney diseases and to define its diagnostic and prognostic role.