

# Plasma Renin Activity in Heart Failure Patients and Chronic kidney disease

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## OBJECTIVES

Chronic heart failure (CHF) and chronic kidney disease (CKD) share common risk factors and pathophysiological pathways, such as atherosclerosis, hypertension, neuroendocrine activation, endothelial dysfunction and inflammation. Impairment of kidney function is frequently observed in CHF; it correlates with clinical and neurohormonal status, and affects prognosis.

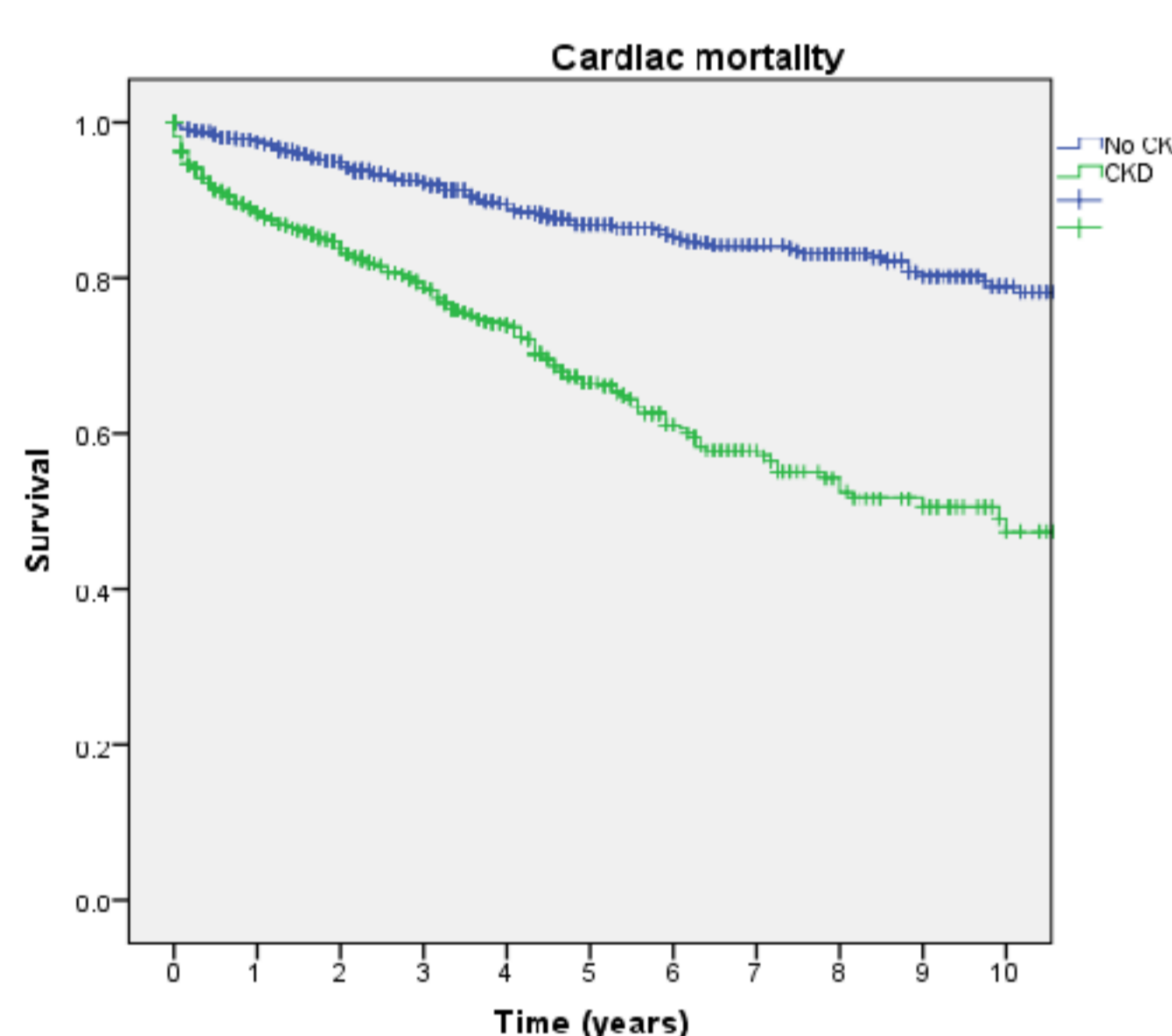
We aimed to identify the prognostic impact of plasma renin activity (PRA) in patients affected by CHF and CKD.

## METHODS

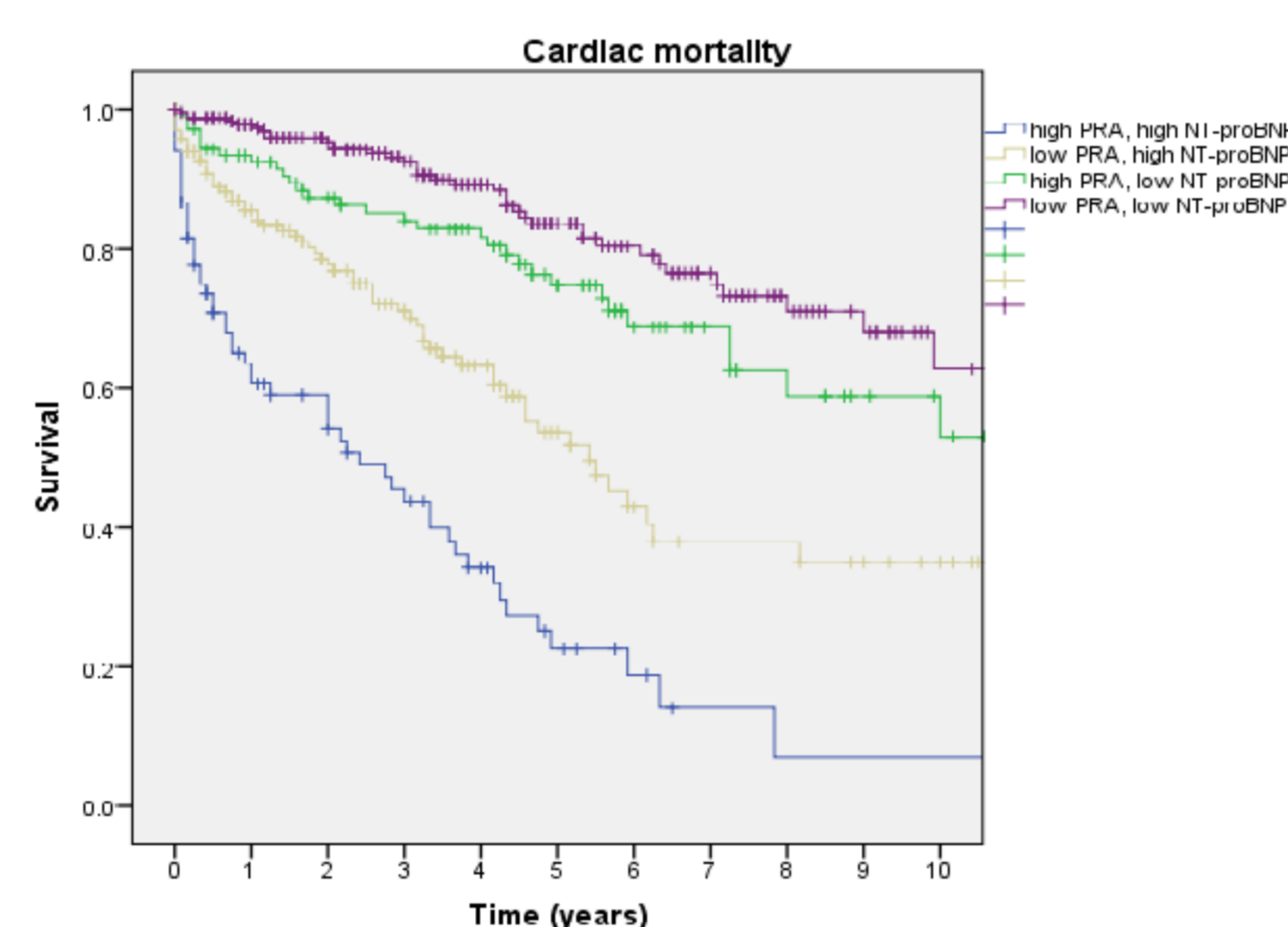
1502 consecutive CHF patients were enrolled (age  $66 \pm 13$  years, mean  $\pm$  SD, left ventricular ejection fraction, LVEF,  $33 \pm 10\%$ ), who underwent a complete clinical and neurohormonal characterization and were then followed-up (median 46 months, interquartile range 20-80 months) for the end point of cardiac death. Glomerular Filtration rate (eGFR) was estimated by the Cockcroft-Gault equation.

## RESULTS

Reduced renal function (eGFR  $\leq 60$  mL/min/1.73 m<sup>2</sup>) was detected in 644 patients (43%), and was associated with worse symptoms, lower LVEF, higher incidence of ischaemic aetiology, diabetes and atrial fibrillation. Higher plasma norepinephrine, NT-proBNP and PRA (all  $p < 0.001$ ) were present in patients with CKD. As compared to patients with preserved renal function, those with CKD had higher cardiac mortality [189 (29%) vs 113 (13.2%),  $p < 0.001$ ]. In CKD patients, at Cox multivariate analysis, only NT-proBNP (1.65, 1.33–2.04,  $p < 0.001$ ) and PRA (1.25, 1.09–1.43,  $p = 0.001$ ) were independent predictors of cardiac death. ROC analysis identified a cut-off value for PRA of 3.98 ng/mL/h that predicted prognosis with the greatest accuracy. Finally, the elevation of both NT-proBNP and PRA identified a subset of patients with the highest risk of cardiac death.



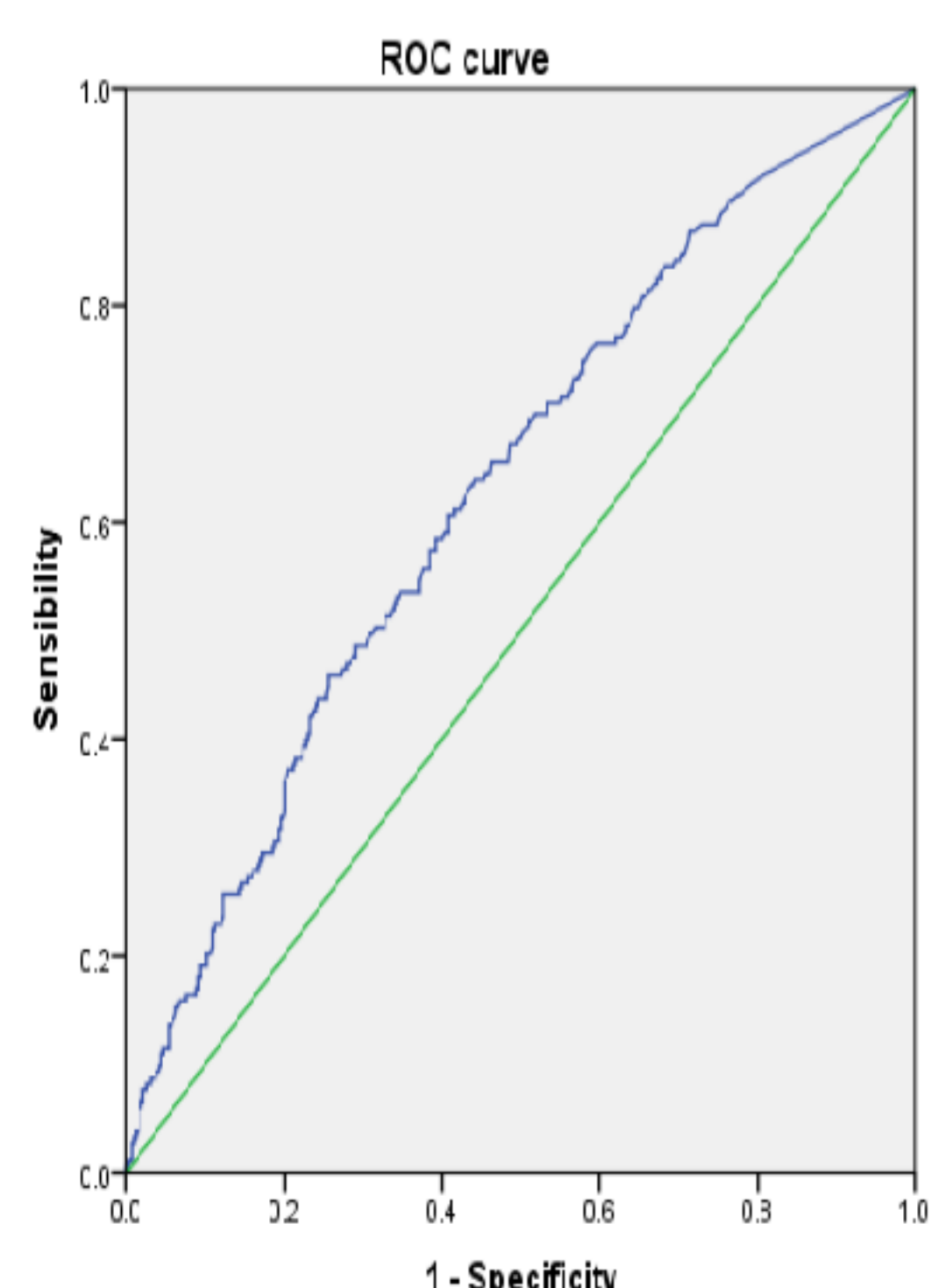
Kaplan-Meier survival curve. Log rank statistic: 96.6,  $P < 0.001$



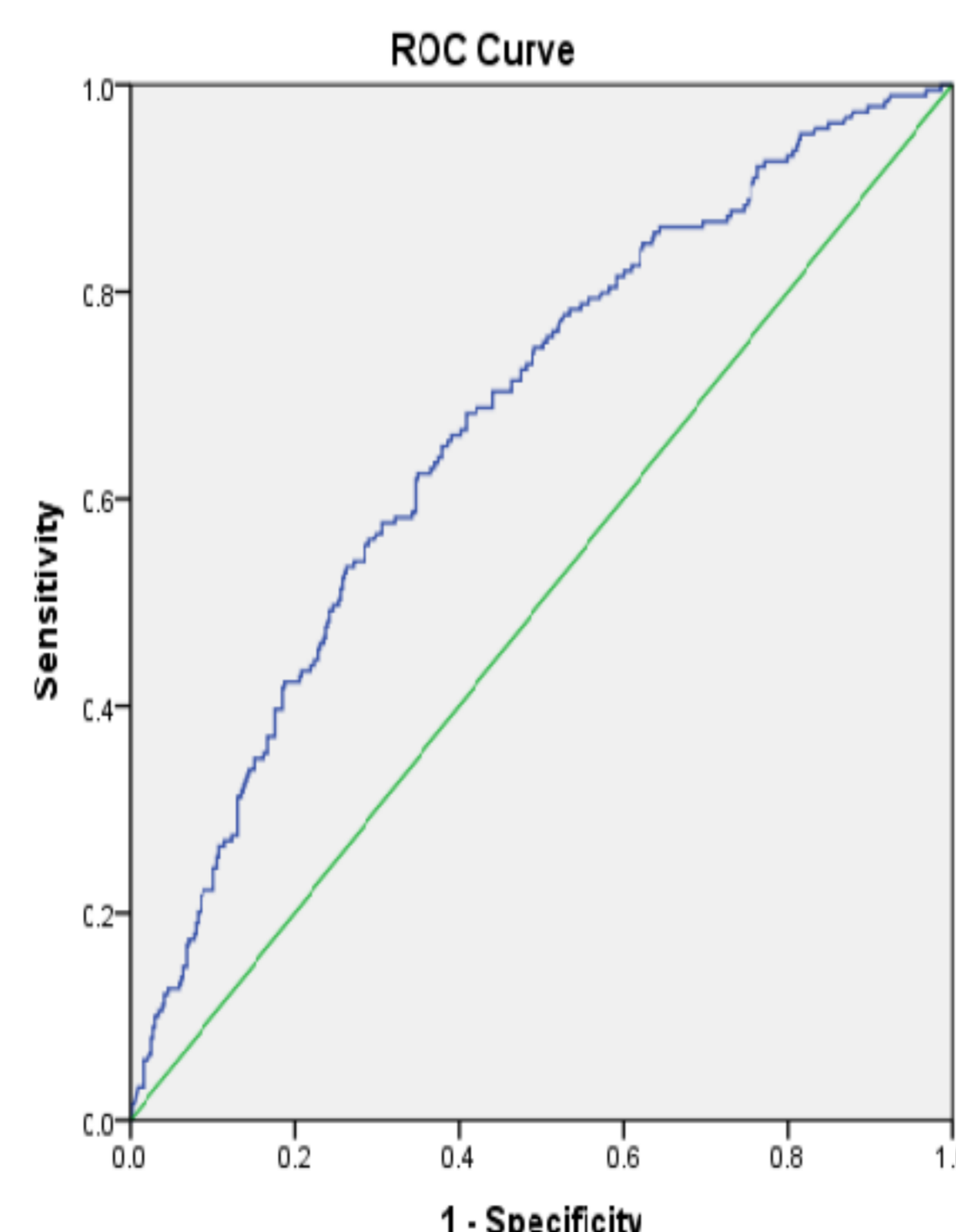
Kaplan-Meier survival curve. Log rank statistic: 134.9,  $P < 0.001$

Baseline demographic and clinical characteristics, as well as neurohormones concentrations in total cohort and in groups without or with chronic kidney disease (CKD).

	Popolazione totale (n=1502)	eGFR>60 (n=858)	eGFR≤60 (n=644)	P
Age (years)	66±13	60±12	74±9	<0.001
Gender F/M, n (%)	397/1105 (26/74)	183/675 (21/79)	214/430 (33/67)	<0.001
BMI (kg/m <sup>2</sup> )	27±11	29±13	25±4	<0.001
LV-EF (%)	33±10	35±9	31±10	<0.001
NYHA class I-II/III-IV, n (%)	944/558 (63/37)	639/219 (75/25)	305/339 (53/47)	<0.001
Ischaemic aetiology, n (%)	646 (43)	310 (36)	336 (52)	<0.001
FA	288 (21)	138 (17)	150 (25)	<0.001
Serum creatinine (mg/dL)	1.23±0.53	0.97±0.21	1.56±0.64	<0.001
eGFR	72±36	95±32	42±11	<0.001
Potassium (mmol/L)	4.0±0.5	4.0±0.5	4.1±0.6	<0.001
Sodium (mmol/L)	138.8±3.0	138.9±2.7	138.7±3.2	0.177
C-reactive protein (mg/dL)	1.10±2.58	0.81±1.85	1.46±3.26	<0.001
Haemoglobin (g/dL)	13.5±1.8	13.9±1.6	12.9±1.8	<0.001
Diabetes, n (%)	401 (27)	207 (25)	193 (31)	0.008
Hypertension, n (%)	758 (51)	398 (47)	360 (57)	<0.001
Dyslipidemia, n (%)	590 (39)	345 (41)	245 (39)	0.478
ACEi/ARBs, n (%)	1112 (74)	667 (78)	445 (69)	<0.001
Beta-blockers, n (%)	1008 (67)	582 (68)	426 (66)	0.401
Antialdosteric, n (%)	686 (46)	372 (44)	314 (49)	0.047
Digoxin, n (%)	415 (28)	213 (25)	202 (32)	0.006
Loop diuretics, n (%)	1026 (68)	534 (63)	492 (77)	<0.001
NT-proBNP (ng/L)	1328 (471-3379)	767 (291-1656)	2868 (1322-6784)	<0.001
PRA (ng/mL/h)	1.2 (0.3-3.9)	0.9 (0.2-2.9)	1.6 (0.4-5.3)	<0.001
Aldosterone (ng/L)	135 (80-214)	128 (79-198)	148 (82-236)	0.008
Epinephrine (ng/L)	29 (10-56)	26 (10-50)	34 (13-63)	<0.001
Norepinephrine (ng/L)	495 (321-733)	421 (277-595)	615 (399-960)	<0.001
ft3 (ng/L)	2.4±0.9	2.6±0.9	2.3±1.0	<0.001
ft4 (ng/L)	12.6±4.6	12.2±4.1	13.2±5.2	<0.001
TSH (mIU/mL)	1.6 (0.9-2.7)	1.5 (0.9-2.5)	1.8 (1.0-3.0)	0.003



ROC analysis for PRA. AUC 0.630,  $P < 0.001$



ROC analysis for NT-proBNP. AUC 0.675,  $P < 0.001$

## CONCLUSIONS

PRA has an independent prognostic value in CHF patients with CKD. The combination of PRA and NT-proBNP identifies a group of high risk patients, who might benefit of a more intensive care, targeted to enhance renin-angiotensin system antagonism.