The clinical impact of plasma leptin levels in a cohort of chronic kidney disease patients

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BACKGROUND

Recent research has clarified the relationship between adipokines, metabolic syndrome (MS) and cardiovascular disease (CVD). The results of animal and clinical studies have revealed a positive relationship between leptin and vascular smooth muscle cell counts and calcification, arterial rigidity, carotid thickness and the incidence of CVD. However, despite leptin fulfilling the definition of a uremic toxin, its exact role in chronic kidney disease (CKD) has yet to be determined.

AIM

The objective of the present study was to investigate putative links between leptin, MS and clinical outcomes by evaluating biochemical and clinical parameters (including vascular calcification scores, inflammatory and bone markers and overall and cardiovascular mortality) in a cohort of stage 2–5D CKD patients.

METHODS

One hundred and forty-two CKD patients (stages 2–5D) participated in this study, and were followed for a minimum of 20 months at Amiens University Medical Center.

RESULTS

Leptin was negatively correlated with the glomerular filtration rate (GFR) (Figure 1), total adiponectin (TAdip) and high-molecular weight adiponectin and positively correlated with age, waist circumference, body mass index (BMI), aortic calcification score (ACS), C-reactive protein (CRP), triglycerides, insulin and parathormone (PTH). Leptin and insulin were significantly correlated with the MS score.

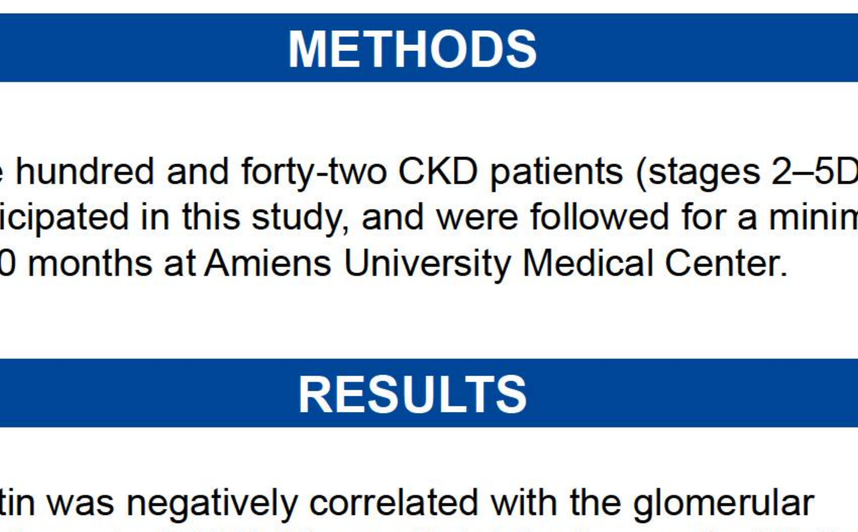


Fig. 1. (A) Serum leptin levels as a function of the CKD stage (*#P < 0.05 when comparing CKD stages 2 and 3 with stages 4 and 5, and when comparing the control group with CKD stages 4 and 5). (B) The linear relationship between serum leptin levels and the estimated GFR, for CKD stages 2–5 ($n = 96$, $r^2 = -0.304$, $P = 0.003$). Control group with apparently normal healthy subjects ($n = 10$).

RESULTS

Tables 1 and 2 show the clinical, demographic and biochemical characteristics of the study population. The BMI, insulin, MS score and PTH were independent predictors of leptin levels (P = 0.002, 0.016, 0.028 and 0.017, respectively). Leptin, insulin and TAdip were independent predictors of the presence of MS (P = 0.05, 0.04 and 0.04) (Table 3). However, leptin levels were not significantly predictive of the clinical outcomes (Figure 2).

Table 1. Clinical and demographic characteristics of the study population[a]

		Leptin		
	All ($n = 142$)	<11.42 ng/mL ($n = 71$)	≥11.42 ng/mL ($n = 71$)	P
Age, years	67 ± 12	65 ± 13	69 ± 12	0.06
Male gender, *n* (%)	86 (60)	56 (79)	30 (42)	0.001
BMI(kg/m²)	28 ± 6	25 ± 5	31 ± 6	0.001
Waist circumference (cm)	100 ± 15	93 ± 13	106 ± 14	0.001
Presence of CVD, *n* (%)	45 (32)	20 (28)	25 (35)	0.471
ACS on CT (%)	3.0 ± 3.0 (1.85)	2.5 ± 2.6 (1.58)	3.5 ± 3.3 (2.32)	0.111
Bone mineral density (HU)	130.4 ± 48.2	132 ± 47	128 ± 50	0.448
Smoking habit, *n* (%)	17 (12)	14 (20)	3 (4)	0.004
Diabetes mellitus, *n* (%)	60 (42)	26 (37)	34 (48)	0.234
Systolic arterial pressure (mmHg)	153 ± 26	150 ± 25	156 ± 27	0.226
Diastolic arterial pressure (mmHg)	81 ± 12	81 ± 13	81 ± 12	0.948
CKD stage, *n* (%)				0.004
2	12 (8)	10 (14)	2 (3)	
3	37 (26)	20 (28)	17 (24)	
4	37 (26)	13 (18)	24 (34)	
5	10 (7)	4 (6)	6 (8)	
5D	46 (32)	24 (34)	22 (31)	

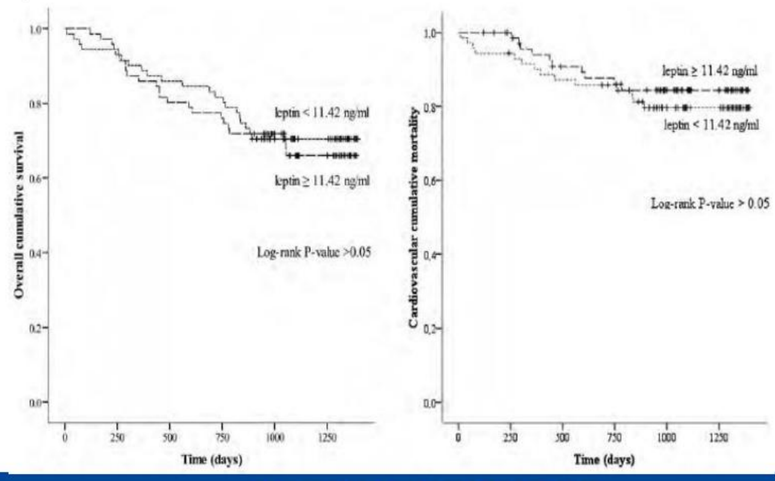
Table 2. Biochemical characteristics of the study population[a]

		Leptin		
	All ($n = 142$)	<11.42 ng/mL ($n = 71$)	≥11.42 ng/mL ($n = 71$)	P-value
GFR[b], mL/min/1.73 m²	35 ± 19	40.42 ± 20.71	30.05 ± 15.76	0.016
Leptin, ng/mL	29.58 ± 36.1 (11.42)	2.79 ± 2.98 (1.82)	56.38 ± 34.15 (43.57)	NA
Total adiponectin, µg/mL	10.56 ± 5.91	11.57 ± 6.42	9.38 ± 5.14	0.031
HMW adiponectin, µg/mL	5.50 ± 4.24	6.29 ± 4.81	4.72 ± 3.46	0.027
Insulin, µU/mL	29.3 ± 23.5	20.6 ± 17.8	38.1 ± 25.3	0.001
Triglycerides, mMol/L	2.03 ± 1.3	1.57 ± 0.8	2.46 ± 1.5	<0.0001
Total cholesterol, mMol/L	4.9 ± 1.1	4.60 ± 1.15	5.12 ± 1.11	0.009
LDL cholesterol, mMol/L	2.62 ± 0.9	2.46 ± 0.8	2.78 ± 0.9	0.04
CRP, mg/L	11.2 ± 24 (3.5)	9.5 ± 19.3 (2.12)	12.9 ± 27.8 (4.26)	0.01
Interleukin-6, pg/mL	5.25 ± 7.9	4.18 ± 4.21	6.24 ± 10.11	0.183
Calcium, mMol/L	2.29 ± 0.18	2.26 ± 0.19	2.31 ± 0.17	0.101
Phosphate, mMol/L	1.28 ± 0.46	1.33 ± 0.53	1.24 ± 0.37	0.212
Intact PTH, pg/mL	137 ± 137 (85)	116 ± 138 (78)	159 ± 135 (121)	0.01
Albumin, g/L	37.4 ± 6.4	36.9 ± 7.2	37.9 ± 5.5	0.506
Haemoglobin, g/dL	12.1 ± 1.7	12.24 ± 1.81	11.94 ± 1.66	0.48

Table 3. Multivariate stepwise linear regression: determinants of serum leptin levels (log-normalized) and the MS score

Items	B (95% CI)	P-value
Leptin levels (log-normalized)[a]		
BMI	0.294 (0.041–0.182)	0.002
Insulin	0.189 (0.002–0.033)	0.028
MS score	0.233 (0.088–0.839)	0.016
PTH	0.198 (0.001–0.005)	0.017
MS score[b]		
Leptin	1.012 (1.000–1.024)	0.05
Insulin	1.020 (1.001–1.040)	0.04
TAdip	0.925 (0.856–0.999)	0.04

Fig. 2



CONCLUSION

Our study was the first to demonstrate a significant, independent link between leptin and MS (but not clinical outcomes) and PTH in patients at different CKD stages. Future studies will have to assess the involvement of leptin in MS and clinical outcomes in CKD, and the potential modulation of leptin by PTH.