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Conicity index as a contributor marker of inflammation in haemodialysis patients

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Abstract

Introduction: **Abdominal fat mass is an important risk factor of inflammation in the general population as it is in haemodialysis (HD) patients. The aim of this study was to investigate the association of adiposity using the conicity index (Ci) with nutritional-inflammatory markers and to analyse whether these factors were related with the clinical outcome in HD patients.**

Methods: **A cross–sectional study in 80 HD patients (men, 65%; aged 68.2 ± 14.2) was carried out. Abdominal fat deposition was evaluated by Ci median with regard to baseline inflammatory, anthropomorphic, and nutritional markers. Linear regression analysis was applied to identify whether serum C-reactive protein (CRP), as an inflammatory biomarker, was an independent predictor of Ci in HD patients.**

Results: **Mean Ci was significantly greater in men ($p = 0.001$). Significant positive correlations were observed between Ci and serum triglycerides ($r = 0.23$; $p < 0.05$) and Ln of serum CRP ($r = 0.27$; $p < 0.01$). A significantly higher median Ci (men ≥ 1.39 and women ≥ 1.33) was observed in inflammated overweight patients by multivariate analysis ($p < 0.05$). Serum CRP, as an inflammatory biomarker, was a significant predictor ($p = 0.021$) of Ci, but its predictive value disappeared after median Ci adjustment of linear regression analysis.**

Conclusion: **Abdominal fat mass, measured by Ci, appears directly linked to inflammation in dialysis. Results support the hypothesis that inflammation in HD patients has pleiotropic effects depending on abdominal body adiposity.**

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Key words: *Conicity index. Abdominal fat deposition. Inflammation. Protein energy wasting. Haemodialysis.*

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EL ÍNDICE DE CONICIDAD COMO MARCADOR CONTRIBUTIVO DE INFLAMACIÓN EN PACIENTES EN HEMODIÁLISIS

Resumen

Introducción: **El depósito de grasa abdominal es un reconocido factor de riesgo de inflamación tanto en la población general como en pacientes en hemodiálisis (HD). El objetivo del estudio fue investigar la asociación de la adiposidad abdominal utilizando el índice de conicidad (Ci) con marcadores nutricionales y de inflamación, y analizar si estos factores se relacionaban con el pronóstico clínico en pacientes en HD.**

Método: **Estudio observacional transversal en 80 pacientes en HD (52 hombres, edad media, 68,2 ± 14,2). El depósito de grasa abdominal fue evaluada por la mediana del Ci con respecto a marcadores inflamatorios, antropomórficos y nutricionales. Aplicación del análisis de regresión lineal para identificar si la proteína C-reactiva (PCR) como biomarcador inflamatorio era uno de los factores predictivos de Ci en la muestra de pacientes en HD.**

Resultados: **La media del Ci era significativamente mayor en hombres que en mujeres ($p = 0,001$). Correlaciones directas fueron observadas entre el Ci y los triglicéridos séricos ($r = 0,23$; $p < 0,05$) y Ln de PCR ($r = 0,27$; $p < 0,01$). En el análisis multivariante aquellos pacientes con mayor mediana de Ci (hombres ≥ 1,39 y mujeres ≥ 1,33) presentaban sobrepeso e inflamación ($p < 0,05$). La PCR como biomarcador de inflamación era un predictor significativo del Ci, aunque el poder predictivo desaparecía cuando se ajustaba por la mediana de conicidad.**

Conclusión: **La aposición de masa grasa abdominal estimada por el Ci está directamente relacionada con el perfil inflamatorio en pacientes en diálisis. Los resultados sustentan la hipótesis de que la inflamación en pacientes en HD tiene efectos pleiotrópicos en función de la adiposidad corporal.**

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Palabras clave: *Índice de conicidad. Grasa abdominal. Inflamación. Malnutrición-inflamación. Hemodiálisis.*

Abbreviations

BIVA: Bioimpedance vector analysis.
BMI: Body mass index.
Ci: Conicity index.
CKD: Chronic kidney disease.
CRP: C-reactive protein.
ESRD: End-stage renal disease.
HD: Haemodialysis.
FM: Fat mass.
FMI: Fat mass index.
Kt/V *urea* (*sp):* Single pool urea kinetic model.
MIS: Malnutrition-inflammation score.
PEW: Protein-energy wasting.
SBW: Standard body weight.
WC: Waist circumference.
WHR: Waist-hip ratio.

Introduction

Abdominal fat mass has been recognized as an important cardiovascular (CV) and renal risk factor in the general population.[1,2] Epidemiological studies have found a progressive increase in the prevalence of cardiovascular risk factors (dyslipidaemia, elevated blood pressure, disturbances in glycaemic control) with increasing body fatness.[3,4] Fat distribution can be assessed by using dual energy X-ray absorptiometry (DXA), computed tomography (CT) or magnetic resonance imaging (MRI) scans[5,6] but the high costs and sophistication of these methods limit their feasibly in clinical practice and other simpler methods have been used.

BMI is the most commonly used and simple measure of overweight and/or obesity[7] but its utility in haemodialysis (HD) patients is controversial.[8] Current clinical nutrition guidelines in chronic kidney disease (CKD) recommend routine BMI measurement, but do not recommend routine assessment of central fat distribution.[9,10] The conicity index (Ci), that includes weight, height and waist circumference (WC) has been proposed as useful index of abdominal adiposity and has demonstrated good association with waist-hip ratio (WHR)[11] and it has been associated at high levels with increased mortality risk in a dialysis population[12]. This has a theoretical range, includes a built-in adjustment of WC for height and weight, and does not require the hip circumference to assess fat distribution. While the BMI predicts the overall fat, WC and the Ci identify the fat located in the central region of the body.[13]

Serum C-reactive protein (CRP) concentration has been widely adopted as a marker of systemic inflammation.[14] Levels of CRP are frequently used in conjunction with assessments of nutritional and inflammatory status to estimate protein energy wasting in end-stage renal (ESRD) patients.[15,16] In addition to being a sensitive surrogate marker of the acute-phase response, an increasing level of CRP may also have direct downstream proinflammatory effects, including activation of complement, tumor necrosis factor alpha (TNF-α), interleukin-1 (IL-1), and especially IL-6. Human adipose tissue was recently shown to be a hormonally active system that secretes a host of inflammatory cytokines including IL-6, which stimulates hepatic production of CRP.[17] In studies of the general population, an association between body fat mass and circulating CRP levels has been confirmed.[18] In particular, visceral adipose tissue distributed within the intraabdominal cavity and surrounding the mesentery and omentum has been shown to be the adipose depot with the greatest contribution to systemic inflammation.[19] This paper hypothesized that the Ci is linked to the inflammation status in HD patients. The aim of this study was to investigate the association of adiposity using the Ci with nutritional-inflammatory markers and to analyse whether these factors were related with the clinical outcome in HD patients.

Subjects and method

Study design

This cross-sectional study was carried out at Hospital Universitario de La Princesa, Madrid (Spain) in 80 HD patients. Informed consent was obtained from every patient prior to inclusion. Eligible participants were adults > 18 years old, and had to be stabilized for a minimum of 3 months before enrolment. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Medical Ethics.

All of the patients underwent regular HD for at least 4 hours three times per week. Biocompatible high-flux dialyzer membranes were utilized and discarded after use. Dialysis adequacy was assessed with regard to the delivered dialysis dose (Kt/V *urea*) using a *single pool (sp)* urea kinetic model. In the present study, patients were stratified on the basis of adjustment by gender. The sample was classified according to median of Ci (men, 1.39; women, 1.33). Forty-six patients (46%) were taking lipid-lowering medications. Most patients were also taking other commonly used drugs in ESRD.

Assessment of nutritional status

The malnutrition-inflammation score (MIS) questionnaire[20] was used to assess nutritional-inflammatory status. MIS includes six different components: three subjective assessments (concerning the patient's history of weight loss, incidence of anorexia and incidence of vomiting) and three objective assessments (subjective grading of muscle wasting, and the loss of subcutaneous fat). In agreement with other studies[21,22] protein energy wasting (PEW) was defined as a MIS score ≥ 5.

Anthropomorphic measurements

To diminish the inter-assay variation coefficients, all anthropometrical measurements were performed by the same researcher. Percent of standard body weight (SBW, %) was calculated as follows: SBW (%) = (actual weight/SBW) x 100, where the patient's weight was the postdialysis weight and the SBW was the weight of Spanish people of the same, sex, height and age range.[23] At the assessment, anthropomorphic measurements were taken (height, weight, BMI, WC and Ci). WC was measured according to WHO guidelines at the mid-point between the lower border of the rib cage and the iliac crest using a rubber measuring tape.[24] BMI was determined as weight (kg) divided by squared height (m^2). The Ci was calculated according to the equation defined by Valdez,[13] which takes into consideration measures of WC, weight and height: WC/[0.109 × square root of (weight/height)]. Ci is based on the volume estimate of the human body constructed to range between the shapes of a cylinder and a double cone assuming a constant body density.[11,13] According to Valdez et al.[13] a Ci of 1.50 means that the individual's WC is 1.5 times bigger than the circumference of a hypothetical cylinder and the theoretically expected range is 1 to 1.73.

Body composition analysis

Body composition was studied by bioimpedance vector analysis (BIVA) (BIVA-101®. Akern-RJL Systems, Florence, Italy) as previously reference method validated in HD patients.[25] On the day of blood collection and 30 minutes after dialysis, measurements were taken using the monofrequency bioelectrical impedance technique. The technique was performed using the distal method, with disposable electrodes (BiatrodesTM 100 S. Akern). Fat mass index (FMI) and lean body mass index (LBMI) were calculated according to the method of Kakiya et al.[26] and expressed as kg/m^2.

Biochemical parameters

Blood was drawn from patients on HD at midweek, prior to the start of the first dialysis session. Blood samples were taken from the arterial site of the vascular access before starting dialysis and heparin administration. CRP was measured by immunoturbidimetry (Roche/Hitachi 904®/Model P: ACN 218, Roche Diagnostics, Basel, Switzerland). Serum albumin was assessed by the bromocresol green method. Other biochemical parameters such as serum prealbumin and lipid profile were assessed by routine laboratory methods, using an automated analyzer (Abbot, Aeroset®, Diamond Diagnosis, Holliston, MA).Variation coefficients were lower than 2%.

Statistical analysis

Student s t-test was used to compare mean values of continuous variables while the Chi-square test for categorical variables. All results are given as mean ± SD. p values ≤ 0.05 were considered statistically significant. Correlations between variables were calculated with the use of Spearman's test. ANOVA was used to analyze differences between the mean of Ci groups. Multivariate analysis of variance (MANOVA) was applied to identify significant interactions between factors. Simple linear regression models were constructed to explore the univariate associations between the Ln CRP (i.e., the CRP level logarithmically transformed to normality using the natural log) and Ci as an independent predictor. Durbin-Watson test was applied. All analyses were performed by using statistical software SPSS version 15.0 for Windows (SPSS®, Inc. Chicago, IL).

Results

Clinical characteristics, nutritional status, and body composition

Demographic and clinical characteristics data of 80 HD patients are showed in table I. Mean Ci ($p < 0.001$) and WC ($p = 0.006$) were significantly higher in men but, non-gender-significant differences were found for BMI. As expected, significant differences in body composition were also noted between the both sexes. Women had a higher percentage of body fat mass ($p < 0.001$) and lower lean body mass (LBM) ($p < 0.001$).

Significant differences on Ln CRP concentration ($p = 0.039$) were shown between men and women. Non-significant differences between sexes were noted in MIS score. Forty nine patients (61.3%) were characterized as protein energy wasting (MIS > 5).

Correlations

A Spearman rank correlation matrix between the 11 investigated variables is given in table II. Results show that Ci was positively and significantly associated with body weight ($r = 0.38$; $p < 0.001$), serum triglycerides ($r = 0.23$; $p < 0.05$) whereas inverse correlation was observed between Ci and HDL-C ($r = -0.40$; $p < 0.001$). Ln CRP concentrations correlated directly and significantly with Ln Ci (fig. 1).

Relation between conicity index median and nutritional inflammatory markers

Results of median of Ci adjusted by sex are summarized in table III. As expected, patients with an increased Ci (abnormal abdominal fat mass), were

Table I
Demographcs and clinical characteristics of 80 haemodialysis patients[a]

	All	*Men*	*Women*	*p-value**
Subjects n (%)	80	52 (65)	28 (35)	0.6
Age (years)	68 ± 14.4	68.2 ± 14.2	67.6 ± 15.1	0.84
DM n (%)	18 (22.5)	13 (25)	5 (17.9)	0.8
Time on HD (months)	42.2 ± 39.6	41.9 ± 40.2	42.6 ± 39.1	0.94
Body weight (kg)	66.5 ± 13.7	69.9 ± 13.2	60.2 ± 12.6	0.002
SBW (%)	98.3 ± 19.2	95.1 ± 15.8	104.3 ± 23.2	0.04
BMI (kg/m^2)	24.9 ± 4.8	24.6 ± 4.3	25.6 ± 5.5	0.38
Waist circumference (cm)	95.2 ± 12.7	98 ± 11.4	89.9 ± 13.4	0.006
TSF (%)	118.2 ± 56.1	116.9 ± 60.1	120.7 ± 48.3	0.77
MAMC (%)	94.3 ± 10.4	93.9 ± 10.3	94.9 ± 10.8	0.69
Fat mass (%)	29.5 ± 10.5	25.7 ± 9.1	36.3 ± 9.6	0.00
Fat mass index (kg/m^2)	7.6 ± 3.7	6.5 ± 3	9.6 ± 4	0.00
Lean body mass (%)	70.5 ± 10.5	74.2 ± 9.1	63.6 ± 9.6	< 0.001
Lean body mass index (kg/m^2)	17.3 ± 2.9	18.1 ± 2.8	15.8 ± 2.3	0.001
Muscle mass (%)	35.3 ± 8.4	36.6 ± 9.2	32.9 ± 6	0.06
Ln MIS (score)	1.94 ± 0.67	1.95 ± 0.74	1.91 ± 0.53	0.77
Plasma glucose (mg/dL)	132.6 ± 59.2	135.8 ± 62.6	127.4 ± 53.8	0.56
Total cholesterol (mg/dL)**	156.5 ± 42.4	149 ± 42.8	170.4 ± 38.7	0.031
Triacylglycerides (mg/dL)	141.6 ± 87.4	149.2 ± 99.8	127.9 ± 60.1	0.3
HDL-C (mg/dL)	52.2 ± 21.2	45.5 ± 15.9	64.7 ± 24.5	< 0.001
LDL-C (mg/dL)	74.8 ± 32.3	71.7 ± 34.1	80.7 ± 28.4	0.25
GGT (UI)	49.1 ± 44.8	55.8 ± 50.6	37.6 ± 30	0.08
Serum albumin (g/dL)	3.7 ± 0.4	3.7 ± 0.5	3.8 ± 0.4	0.42
Serum prealbumin (mg/dL)	26.5 ± 8.6	26.5 ± 9.5	26.5 ± 7	0.99
Ln CRP (mg/dL)	-0.21 ± 1.2	0.01 ± 1.2	-0.60 ± 1.27	0.039
Systolic Blood pressure (mmHg)	126.8 ± 20	126.6 ± 19.4	127.3 ± 21.9	0.89
Diastolic Blood pressure (mmHg)	70 ± 11.3	69.1 ± 10.5	73 ± 12.3	0.15
Conicity index	1.37 ± 0.1	1.40 ± 0.1	1.31 ± 0.09	0.001
Charlson index (score)	8.0 ± 2.9	8.2 ± 3.1	7.7 ± 2.7	0.54
Kt/V urea (sp)	1.34 ± 0.4	1.3 ± 0.4	1.46 ± 0.4	0.07
PEW[†] n (%)	49 (61.3)	32 (61.5)	17 (60.7)	0.94

*P-values are based on Chi-square test or Student's t-test.
BMI: Body mass index; DM: Diabetes mellitus; HD: Hemodialysis; HDL-C: High density lipoprotein; Kt/V urea (sp): Urea kinetic model; LDL-C: Low density lipoprotein; Ln CRP: Natural logarithm of C-reactive protein; Ln MIS: Natural logarithm of malnutrition-inflammation score; PEW: Protein energy wasting; SBW%: Percentage of standard body weight; TSF %: Percentage of triceps skinfold thickness.
**47.4% of the patients were taking lipid-lowering medications.
[†]PEW was defmed by MIS score > 5.

more prevalent on HD and tended to be older. BMI ($p = 0.04$) and triceps skinfold thickness ($p = 0.06$) tended to increase with the Ci. SBW ($p = 0.04$), fat mass ($p < 0.01$), and fat mass index ($p < 0.01$) were greater in high median Ci group. However, these patients tended to be more wasted (MIS > 5) and to have reduced levels of serum albumin ($p = 0.07$) and prealbumin ($p < 0.05$) whereas serum Ln CRP was significantly increased ($p < 0.05$). Significant interactions were observed between median of Ci with anthropomorphic measures (BMI, WC, TSF, fat mass, FMI, muscle mass) (at least, $p < 0.05$) and biochemical parameters (serum prealbumin and CRP) (all, $p < 0.05$) by multivariate analysis (table III).

Inflammation as a predictor of abdominal fat mass

To evaluate the independent relation between abdominal fat mass and serum CRP concentrations two forward linear regression models were performed (table IV). Model 1 included Ci as independent variable adjusted by sex and age, while linear regression Model 2 included Ci (high or low Ci) as a dummy inde-

Table II
Spearman rank correlation matrix for 11 variables in 80 hemodialysis patients

	Age	*Body weight*	*BMI*	*Waist circumference*	*FM (%)*	*FMI*	*Conicity index*	*TAG*	*HDL-C*	*Ln MIS*	*Ln CRP*
Age (years)											
Body weight (kg)	-0.11										
BMI (kg/m^2)	0.06	0.75[c]									
Waist circumference (cm)	0.04	0.80[c]	0.65[c]								
Fat mass (%)	0.34[b]	0.12	0.38[c]	0.23[a]							
Fat mass index (kg/m^2)	0.28[b]	0.35[c]	0.63[c]	0.43[c]	0.93[c]						
Conicity index	0.13	0.38[c]	0.17	0.79[c]	0.11	0.16					
Triacylglycerol (mgldL)	-0.02	0.32	0.33[b]	0.36[c]	0.17	0.23[b]	0.23[a]				
HDL-C (mgldL)	0.04	-0.24[a]	-0.10	-0.34[c]	-0.001	-0.02	-0.40[c]	-0.22[a]			
Ln MIS	0.20	-0.42[c]	-0.49[c]	-0.16	-0.12	-0.24[a]	0.19	-0.12	-0.22[a]		
Ln CRP (mgldL)	0.08	0.06	-0.02	0.16	-0.07	-0.06	0.27[b]	0.24[a]	-0.24[a]	0.37°	

The anthropometrics variables.
BMI: Body mass index; FM: Fat mass; FMI: Fat mass index; HDL-C: High density lipoprotein cholesterol; Ln CRP: Natural logarithm of C-reactive protein; Ln MIS: Natural logarithm of malnutrition-inflammation score; TAG: Serum triacylglycerides.
[a]$p < 0.05$.
[b]$p < 0.01$.
[c]$p < 0.001$.

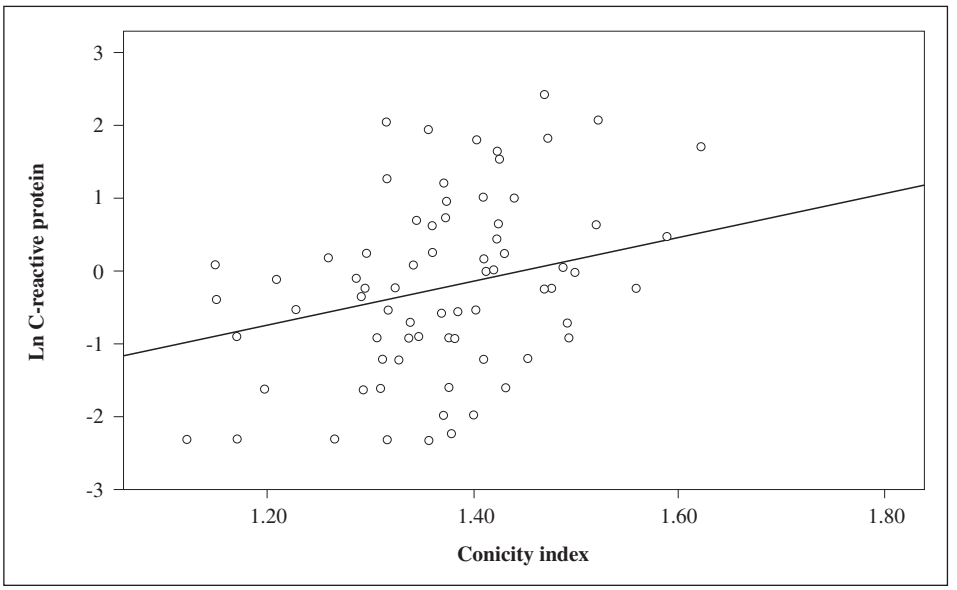

Fig. 1.—Relationship between natural logarithm of C-reactive protein (Ln CRP) and conicity index in 80 haemodialysis patients (R = 0.25; p = 0.021).

pendent variable. Durbin-Watson tests were 0.85 in both of them. Only in Model 1, Ci was significantly associated with Ln CRP (p = 0.021).

Discussion

In the present study, high Ci was associated with increased concentrations of CRP suggesting that abdominal fat deposition is a significant source of CRP production in HD patients. Serum CRP, as an inflammatory biomarker, was a significant predictor of Ci, but its predictive value disappeared after median Ci adjustment in the linear regression analysis. While CKD patients being overweight may be interpreted as a protective factor and better nutritional status markers due to the "reverse epidemiology paradox", abnormal fat deposition may be detrimental due to its contribution to metabolic disturbances.

In the current study, in a similar way that previously described in non-HD subjects,[27] HD-women showed lower Ci than HD-men. The implications of sex interactions on some inflammatory markers are unclear but women showed lower Ci than men due to differences in fat distribution. These results pushed us to study present HD population according to their Ci median adjusted for sex.

BMI, which is a measure of body composition, does not distinguish between muscle and fat mass, and may

Table III
Demographcs and clinical characteristics of 80 haemodialysis according to median of central fat deposition evaluated by the conicity index (CI)

	Low median CI (n = 40)	*High median CI (n = 40)*	*p-value**
Age (years)	66.1 ± 16.2	70.9 ± 11.9	0.07
Time on HD (months)	39.1 ± 34.1	45.2 ± 44.7	0.49
Body weight (kg)	63.9 ± 11.6	69 ± 15.2	0.02
SBW (%)	93.9 ± 15.2	102.7 ± 21.6	0.04[a]
BMI (kg/m^2)	24.0 ± 3.9	25.9 ± 5.4	0.08[a]
Waist circumference (cm)	88.2±10.2	102.1 ± 11.1	0.00[c]
TSF (%)	106.8 ± 44.6	130 ± 64.3	0.06[a]
MAMC (%)	95.2 ± 9.9	93.3 ± 10.9	0.43
Fat body mass (%)	26.5 ± 9.8	32.5 ± 10.5	0.01[b]
Fat mass index (kg/m^2)	6.4 ± 2.7	8.7 ± 4.2	0.005[b]
Lean body mass (%)	73.5 ± 9.9	67.5 ± 10.5	0.01
Lean body mass index (kg/m^2)	17.5 ± 3.2	17 ± 2.4	0.45
Muscle mass (%)	38 ± 8.7	32.5 ± 7.1	0.003[b]
Ln MIS (score)	1.8 ± 0.71	2.08 ± 0.6	0.05
Plasma glucose (mg/dL)	125.9 ± 46.5	139.9 ± 70.5	0.32
Total cholesterol (mg/dL)**	163.1 ± 44.1	150 ± 40.2	0.16
Triacylglycerides (mg/dL)	142.7 ± 105.5	140.5 ± 67	0.91
HDL-C (mg/dL)	56.9 ± 20.1	47.3 ± 21.5	0.04
LDL-C (mg/dL)	80.2 ± 35.3	69.5 ± 28.4	0.15
GGT (UI)	45.1 ± 41.9	52.8 ± 47.7	0.45
Serum albumin (g/dL)	3.8 ± 0.4	3.6 ± 0.5	0.07
Serum prealbumin (mg/dL)	28.5 ± 9	24.3 ± 7.6	0.03[a]
Ln CRP (mg/dL)	-0.48 ± 1.23	0.04 ± 1.23	0.05
Systolic Blood pressure (mmHg)	128.7 ± 20.8	124.9 ± 19.6	0.43
Diastolic Blood pressure (mmHg)	71.8 ± 11.5	69.3 ± 11	0.35
Charlson index score	7.6 ± 3.1	8.5 ± 2.7	0.54
Kt/V urea *(sp)*	1.3 ± 0.5	1.4 ± 0.3	0.17
PEW[†] n (%)	22 (55.5)	27 (67.5)	0.25

*P-values are based on Chi-square test or ANOVA test according median of conicity index (Ci); Median of conicity index was defined as follows: low Ci group (men < 1.39; women < 1.33) and high Ci group (men ≥ 1.39; women ≥ 1.33).
[a,b,c]P-values within the means of Ci bearing different letters were significantly different; [a]($p < 0.05$); [b]($p < 0.01$); [c]($p < 0.001$) (MANOVA).
BMI: Body mass index; DM: Diabetes mellitus; HD: Haemodialyysis; HDL-C: High density lipoprotein; Kt/V urea *(sp):* Urea kinetic model; *LDLC:* Low density lipoprotein; Ln CRP: Natural logarithm of C-reactive protein; Ln MIS: Natural logarithm of malnutrition-inflammation score; PEW: Protein energy wasting; SBW%: Percentage of standard body weight; TSF %: Percentage of triceps skinfold thickness.
**46% of the patients were taking lipid-lowering medications.
[†]PEW was defined by MIS score > 5.

be obscured by imbalances in fluid homeostasis in this population. Some significant relationships between BMI, Ci and Ln CRP among dialysis patients were found in the current study. However, Ci was positively correlated with both serum triglycerides and Ln CRP and inversely with plasma HDL-C, suggesting relationships between abdominal adiposity and metabolic risk factors. Arimura et al.[28] showed that WC is a better predictor of changes in HDL-C than BMI.

Ci may be a useful parameter to identify individuals with abdominal adiposity but who are not necessarily obese/overweight. Our findings highlight that abdominal fat distribution measured by Ci rather than body fatness has the dominant influence on CRP levels. Several studies have shown that inflammatory biomarkers, such as CRP,[29] white blood cells[30] and IL-6,[29,31] are strong independent predictors of all-cause and CV mortality in ESRD patients. This suggests that inflammation plays a pivotal role in the development of both PEW and atherosclerosis in this population. Inflammation when associated to obesity is thought to derive from the adipose tissue itself. Association between body fat mass and circulating CRP levels has been confirmed in studies on the general population.[18] Moreover, recent studies have shown that adipose tissue in obesity is characterized by macrophage infil-

Table IV
Inflammatory biomarker in a linear regression analysis as likely predictor in 80 haemodialysis patients

Variable	Ln CRP			
	Coefficient	*SEM*	*p-value*	*95% CI*
Model 1†				
Conicity index	2.94	1.25	0.021	-7.68 to -0.83
Constant	-4.25	1.72	0.015	0.46 to 5.43
Model 2‡				
Median conicity index	0.50	0.27	0.06	-0.030 to 1.044
Constant	-0.46	0.19	0.017	-0.84 to -0.087

Ln CRP: Natural logarithm of C-reactive protein; SEM: Standard error of the mean; 95% CI: 95% confidence interval.
†Model 1: Conicity index as a continuous independent variable (R = 0.25).
‡Model 2: Median conicity index as a dummy variable adjusted by sex (R = 0.20).

tration[32] and that weight loss is associated with a reduction in circulating concentrations of inflammatory biomarkers, such as IL-6[33] and CRP.[34] These results suggest that body fat, in particular abdominal fat deposition, when interpreting the significance of an elevated CRP level in HD patients, should be considered.

When examining the relationship between median Ci cut-off point for increased risk and other risk factors, a high Ci was significantly associated with disturbances in lipoprotein profile and body adiposity. Furthermore, in the current report the finding that HD patients with increased Ci also have a higher prevalence of PEW, decreased mid-arm muscle circumference (MAMC) and lower levels of serum albumin and prealbumin concentrations was taken into account. Beddhu et al.[35] reported that a protective effect from a high BMI is only present in patients with a normal or high muscle mass. In agreement with Honda et al.[36] it was observed that overweight patients with PEW were characterized by increased fat body mass, low lean body mass, and inflammation. Interestingly, it seems paradoxical that 61% of HD patients showed increased fat mass and surrogate markers of sarcopenia. Inflammatory biomarkers such as IL-6, especially, have been speculated to play a central role in the loss of muscle mass (sarcopenia), which is often observed in ESRD patients.[36] In the present study, CRP was correlated with nutritional status (MIS), which indicates an important role for the systemic inflammation in the development of PEW in ESRD.

Ci has been shown to be related to cardiovascular risk in the general population. Almeida et al.[27] reported that Ci had the highest sensitivity and specificity for predicting the occurrence of cardiovascular risk factors in non-HD patients. Long-term prospective studies are needed to evaluate the evolution of inflammatory biomarkers and their relation to changes in regional body composition in HD patients.

Several limitations of the current study must be acknowledged. First, only one single measurement of CRP (non-hs) was used in the present study, even though inflammatory biomarkers may vary with time. Second, the influence of hormones could modify the association, since an inverse relationship between testosterone and CRP levels has been reported.[37] Estrogen deficiency has also been associated with elevated CRP levels, independent of body fat.[38] Although the adipose tissue has been implicated in inflammatory cytokine production, visceral fat appears to have the greatest potential to express cytokines that induce hepatic CRP expression.[17] Moreover, our cross-sectional study did not permit the assessment of how changes in obesity parameters affect CRP levels. In addition, IL-6 levels were not available, so we were unable to assess whether IL-6 impacts the relationship between overweight/obesity and CRP. Finally, the cross-sectional design of our study limits the ability to ascribe causal relationships to the associations detected.

Our results are relevant to the current discussion on whether or not being overweight and obesity are protective in patients with predictive power of abdominal fat which was largely independent of inflammation as measured by high CRP. Ci seems to be a good indicator of fat distribution, by detecting changes in body composition, and thus permitting comparisons between subjects who present different body weight and height measurements.

In conclusion, the present study demonstrated association between body fat, in particular abdominal fat mass, and serum CRP concentrations in HD patients. CRP levels increased to a greater degree with variation in fat quantity and are more affected by fat distribution in men compared with women. Adiposity as a contributor of subclinical inflammation may be particularly relevant in HD patients. These findings underscore the importance of incorporating evaluation of one measurement of abdomimal fat, as Ci, in addition to the BMI in clinical practice. Additional studies are required to determine whether the anthropometric measures (WC, Ci, WHR) are sensitivity parameters to determine an increase of CV health risk in HD patients.

Statement of authorship

All authors have significantly contributed to the paper, had access to all the data in the study and approved the final version of the manuscript to be submitted for publication. MR is the corresponding author and guarantor and the paper and has contributed to the study design, data analysis, discussion and writing of the paper. GB and FJS-M have contributed to the data analysis and writing of the paper.

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