

Adiponectin correlates with body mass index and to a lesser extent with left ventricular mass in dialysis patients

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Abstract

Background: Adiponectin is a serum protein produced by adipose tissue which exerts anti-inflammatory, anti-diabetic and anti-atherosclerotic properties, hence is considered a cardio-protective marker. With the current uncertain role of adiponectin in dialysis patients to the aim of this study was to investigate its relationship with left ventricular (LV) structure and function in these patients.

Methods: This study included 89 (age 56 ± 13 years, 43% male) patients treated with regular dialysis for > 6 months, and 55 control subjects with normal renal function. A complete two-dimensional, M-mode and tissue-Doppler echocardiographic study, and biochemical blood analyses, adiponectin and anthropometric parameters were obtained on the same day.

Results: Dialysis patients had lower body mass index (BMI) and lower body surface area (BSA) ($p < 0.001$ for both), lower waist/hips ratio ($p = 0.005$), higher LV mass index (LVMI, $p < 0.001$), higher adiponectin level ($p < 0.001$) and LV end-systolic volume ($p = 0.003$), lower LV ejection fraction ($p = 0.006$), longer isovolumic relaxation time ($p < 0.001$), lower mean LV strain ($p = 0.002$), larger left atrium volume ($p = 0.022$) and lower left atrium emptying fraction ($p = 0.026$), compared to controls. In dialysis patients, adiponectin correlated with waist circumference ($r = -0.427$, $p < 0.001$), BMI ($r = -0.403$, $p < 0.001$) and BSA ($r = -0.480$, $p < 0.001$), and to a lesser extent with LVMI ($r = 0.296$, $p = 0.005$), waist/hips ratio ($r = -0.222$, $p = 0.037$) and total cholesterol ($r = -0.292$, $p = 0.013$). But in controls, it correlated only modestly with age ($r = 0.304$, $p = 0.024$), hemoglobin ($r = 0.371$, $p = 0.005$), high density lipoprotein cholesterol ($r = 0.315$, $p = 0.019$) and LVMI ($r = 0.277$, $p = 0.043$).

Conclusions: It seems that in dialysis patients, adiponectin modest correlation with anthropometric measurements suggests an ongoing catabolic process rather than a change in ventricular function. (Cardiol J 2018; 25, 4: 501–511)

Key words: adiponectin, dialysis, left ventricular mass, body mass index

Introduction

Adiponectin, an adipocyte-derived hormone, is a serum protein produced by the adipose tissue [1, 2], and exerts anti-inflammatory, anti-diabetic and anti-atherosclerotic properties [3–6], and hence is considered a cardio-protective marker. Several

previous studies suggested a possible influence of adiponectin in many clinical conditions, such as obesity, insulin resistance, hypertension, dyslipidemia and atherosclerotic heart disease [7–11]. Hypoadiponectinemia has been identified as independent risk factor for cardiovascular (CV) disease [12, 13]. Adiponectin prevents progression of left

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ventricular (LV) hypertrophy (LVH) [4, 14], which correlates with CV complications both in hypertensive [15, 16] and chronic kidney disease (CKD) [17, 18]. While, it was found to normally correlate with blood pressure values, such a relationship in hypertensives remains controversial [11, 19–22]. On the other hand, adiponectin levels have been found to correlate with LV mass index (LVMI) [4, 23], and with impaired renal function [24–26], in patients with renal failure and those treated with dialysis, although modestly [24, 27]. The aim in this study therefore, was to investigate the relationship between adiponectin and LV structure and function measurements in dialysis patients, as an attempt to get more insight into its protective CV role in these patients.

Methods

Patients

Eighty-nine consecutive patients treated with regular dialysis at the Dialysis Unit of the University Clinical Centre of Kosovo were included in this study (age 56 ± 13 [18–80] years, 43% male) and 55 subjects, who had normal renal function, and served as a control group which was recruited between May 2013 and April 2016. All subjects gave informed consent to participate in the study, which was approved by the Ethics Committee of Medical Faculty, University of Prishtina. All patients included had been receiving chronic standardized dialysis 500–750 mL/min dialysate flow, 250–300 mL/min blood flow, over 3–4 h session, 3 times per week, for at least 6 months prior to recruitment in the study. The dialysis potassium level was 2.0 mEq/L and calcium level was 1.75 mEq/L. Patients with active malignancy, decompensated heart failure, hepatic or pulmonary disease, pregnant women and those with failed transplant were excluded from the study. Blood pressure was recorded with a brachial sphygmomanometer after subjects had rested in the supine position for at least 10 min.

Clinical data

For all participants, demographic details, physical examination and anthropometric measurements were taken. Hypertension was defined as systolic blood pressure ≥ 140 mmHg, and/or diastolic blood pressure ≥ 90 mm Hg, or when patients were using antihypertensive therapy. Diabetes was defined as fasting plasma glucose ≥ 126 mg/dL (> 7 mmol/L) or the use of hypoglycemic medications. Body mass index (BMI) was measured after the dialysis session and was calculated by dividing

dry weight by body height (kg/m^2). Twelve lead electrocardiogram was also recorded in all patients and QRS duration was measured.

Blood analysis

Blood urea nitrogen, creatinine, albumin, total protein, total cholesterol, triglyceride, calcium, phosphate, iron, hematocrit and hemoglobin were measured using standard methods. High density lipoprotein cholesterol (HDL-L) was measured by homogeneous enzymatic colorimetric assay (COBAS INTEGRA[®] 400 plus, Roche), parathyroid hormone by immunoassay (COBAS e 411 analyzer-Roche) and C-reactive protein (CRP) by particle enhanced turbidimetric assay (COBAS INTEGRA[®] 400 plus, Roche). All samples for a given assay were tested simultaneously, in duplicate and in appropriate dilutions, according to conventional protocols.

Adiponectin measurement

Venous blood samples were withdrawn from each subject after ≥ 8 h of fasting. The samples were stored at -80°C until analyzed. Serum adiponectin concentration was measured by ELISA Microplate Reader Gea Linear. Intra- and inter-assay coefficient of variation was below 3.0% and 5.1%, respectively [28].

Cardiac structure and function:

Left ventricular structure measurements.

Echocardiographic examination in all patients and in controls was performed on the same day of dialysis using a Philips iE33 system with a multi-frequency transducer and harmonic imaging as appropriate. Images were obtained with the patient in the left lateral decubitus position and during quiet expiration. LV volumes and ejection fraction (EF) were calculated from the apical 2- and 4-chamber views using the modified Simpson method. Left ventricular mass (LVM) was estimated using the anatomically validated formula of Devereux et al. [29, 30] and was indexed to height^{2.7} (LVMI) [31]: $\text{LVM [g]} = 0.8 \times (1.04 \times (\text{LVEDD} + \text{PWTD} + \text{IVSTD})^3 - (\text{LVEDD})^3) + 0.6$ [30]. LVH was defined as a LVMI of $47 \text{ g/m}^{2.7}$ for women and $53 \text{ g/m}^{2.7}$ for men [32]. LVM normalized for body surface area (LVM/BSA) was also calculated as g/m^2 .

Left ventricular function measurements.

From the spectral wave Doppler LV filling, peak E wave velocity, peak A wave velocity, the ratio between peak E and A velocities (E/A ratio), and E wave deceleration time were measured. From tissue-Doppler imaging recordings, peak systolic (s'),

and early diastolic (e') and late diastolic (a') mitral annular velocities were also measured. The ratio of trans-mitral to myocardial early diastolic peak velocity (E/e') was calculated, after averaging septal and lateral e' velocities [33, 34], to reflect filling pressures. Mitral annular plane systolic excursion (MAPSE) was measured by placing the M-mode cursor at the lateral and septal angles.

Total LV filling time (FT) was measured from the onset of the E wave to the end of the A wave and ejection time (ET) from the onset to the end of the aortic Doppler flow velocity. Total isovolumic time (t-IVT) was calculated as $60 - (\text{total ET} + \text{total FT})$ and was expressed in s/min [35]. Tei index was calculated as the ratio between t-IVT and ET [36]. LV isovolumic relaxation time (IVRT) was measured as the time interval between LV end-ejection (from the pulsed-wave Doppler recording of the outflow tract velocity) and the onset of transmitral E-wave velocity.

The diameter of the LV outflow tract (LVOT) was measured from the parasternal long axis view as the distance between the bases of the aortic valve cusp during systole. The LVOT area was then calculated using the formula: $\text{LVOT area} = [(\text{LVOT diameter average}/2)^2] \times 3.14$.

The average velocity time integral (VTI) was measured using the pulsed wave Doppler samples obtained at the center of the LVOT from the apical view. The stroke volume was calculated as the product of the LVOT area and the VTI of the LVOT blood flow.

Left atrial (LA) measurements. LA diameter was measured from aortic root recordings with the M-mode cursor positioned at the level of the aortic valve leaflets. LA volumes were measured using area-length method from the apical four chamber views, according to the guidelines of the American Society of Echocardiography and European Association of Echocardiography [22, 37]. Left atrial maximal volume (LAV max) was measured at the end of LV systole, just before the opening of the mitral valve, LA minimal volume (LAV min) was measured at end diastole, immediately after mitral valve closure. LA total emptying fraction was calculated using the formula [38]: $\text{LA total emptying fraction} = \text{LAV max} - \text{LAV min}/\text{LAV max} \times 100$.

Statistical analysis

Values are expressed as means \pm standard deviation. Differences between the two groups were analyzed using the unpaired Student *t* test

following the analysis of variance. P values < 0.05 were considered statistically significant. The χ^2 test was used to compare the categorical variables. Pearson correlations were performed to identify the simple correlations between adiponectin and the other variables. Subjects were stratified into four groups based on the dialysis treatment and on the presence of LVH on the echocardiographic examination: Group 1 (dialysis patients with LVH), Group 2 (dialysis patients without LVH), Group 3 (non-dialysis patients with LVH) and Group 4 (non-dialysis patients without LVH). A one-way ANOVA with Bonferroni correction was performed to compare continuous variables. All analyses were performed using SPSS 22 for windows.

Results

Clinical data of dialysis patients versus controls (Table 1)

The baseline demographic, anthropometric and clinical data of dialysis patients and controls are shown in Table 1. The age, gender and CV risk factors (smoking, diabetes, arterial hypertension and cholesterol level) were not different between groups. The dialysis patients had lower BMI and lower BSA ($p < 0.001$ for both), smaller waist measurements ($p < 0.001$), smaller inter-hip distance ($p = 0.002$), lower waist/hip ratio ($p = 0.005$), higher SBP and DBP ($p = 0.002$ and $p = 0.018$, respectively), higher baseline heart rate, higher CRP level, lower red blood cell (RBC), lower hemoglobin, lower albumin level, lower hematocrit and higher adiponectin level ($p < 0.001$, for all), lower blood iron level ($p = 0.028$), and higher fasting glucose ($p = 0.005$) compared to controls. Less dialysis patients were treated with beta-blockers ($p < 0.001$), and more treated with angiotensin converting enzyme inhibitors ($p = 0.003$) and calcium antagonists ($p < 0.001$), compared to controls.

Cardiac function of dialysis patients versus controls (Table 2)

Dialysis patients had higher LVMI ($p < 0.001$), thicker interventricular septum ($p = 0.006$), larger LV end-systolic volume ($p = 0.003$), lower LVEF ($p = 0.006$), shorter LVET ($p < 0.001$), longer IVRT ($p < 0.001$), lower Tei index ($p = 0.003$), lower septal MAPSE ($p = 0.036$), higher A wave ($p = 0.009$), lower septal e' ($p = 0.017$), larger LA volume ($p = 0.022$) and lower LA emptying fraction ($p = 0.026$), compared to controls.

Table 1. Clinical and biochemical data in dialysis patients versus controls.

Variable	Controls (n = 55)	Dialysis patients (n = 89)	P
Age [years]	55 ± 13	56 ± 13	0.839
Gender [male, %]	56	43	0.111
Smoking [%]	31	20	0.146
Diabetes [%]	11	18	0.252
Hypertension [%]	40	56	0.059
SBP [mm Hg]	141 ± 20	153 ± 24	0.002
DBP [mm Hg]	87 ± 10	82 ± 13	0.018
Beta-blockers [%]	29	5.6	< 0.001
ACE-inhibitor [%]	24	47	0.003
Rocaltrol [%]	0	95	< 0.001
Calcium carbonate [%]	4	98	< 0.001
Aspirin [%]	42	9	< 0.001
Ca-channel blockers [%]	2	29	< 0.001
Diuretic [%]	20	10	0.096
Heart rate [bpm]	73 ± 10	80 ± 13	< 0.001
Waist [cm]	96 ± 11	88 ± 12	< 0.001
Hips [cm]	105 ± 11	99 ± 12	0.002
Waist/hip ratio	0.92 ± 0.06	0.89 ± 0.05	0.005
Weight [kg]	80 ± 13	67 ± 14	< 0.001
Body mass index [kg/m ²]	27 ± 3.4	24 ± 4.4	< 0.001
Body surface area [m ²]	1.1 ± 0.2	0.9 ± 0.2	< 0.001
Adiponectin [μg/mL]	5.9 ± 3	15 ± 9	< 0.001
C-reactive protein [mg/L]	3.4 ± 3	11 ± 20	< 0.001
HDL-cholesterol [mmol/L]	1.0 ± 0.5	0.9 ± 0.3	0.097
Total cholesterol [mmol/L]	4.8 ± 0.8	4.5 ± 0.9	0.108
Triglyceride [mmol/L]	1.6 ± 0.5	1.8 ± 0.8	0.030
Creatinine [umol/L]	80 ± 16	711 ± 160	< 0.001
Blood urea nitrogen [mmol/L]	5.4 ± 1.4	27 ± 5.3	< 0.001
Parathormone [pg/mL]	39 ± 26	126 ± 114	0.012
Phosphorus [mg/dL]	1.0 ± 0.07	1.6 ± 0.5	< 0.001
Total calcium [mmol/L]	2.2 ± 0.15	2.1 ± 0.3	0.428
Iron [μmol/L]	19 ± 4.9	16 ± 8.3	0.028
Fasting glucose [mmol/L]	5.6 ± 1.5	6.9 ± 3.9	0.005
Total protein [g/L]	66 ± 2.6	65 ± 5.4	0.438
Albumin [g/L]	40 ± 4	37 ± 4	< 0.001
Aspartate aminotransferase [U/L]	18 ± 6	20 ± 16	0.291
Alanine aminotransferase [U/L]	20 ± 8	23 ± 21	0.148
Red blood cells × 10 ⁶ /L	4.5 ± 0.6	3.5 ± 0.9	< 0.001
White blood cells × 10 ³ /L	7.7 ± 1.3	7.5 ± 3.2	0.594
Hemoglobin [g/dL]	14 ± 1.3	10 ± 1.6	< 0.001
Hematocrit [%]	39 ± 6.1	33 ± 5.5	< 0.001

SBP — systolic blood pressure; DBP — diastolic blood pressure; ACE — angiotensin converting enzyme; HDL — high-density lipoprotein

Table 2. Echocardiographic data in controls group vs. dialysis patients.

Variable	Controls (n = 55)	Dialysis patients (n = 89)	P
LV dimension and mass			
LV mass [g]	214 ± 75	230 ± 66	0.201
LV mass index [g/m ^{2.7}]	47 ± 13	68 ± 29	< 0.001
Inter ventricular septum [cm]	1.2 ± 0.16	1.25 ± 0.2	0.006
LV posterior wall [cm]	1.0 ± 0.1	1.1 ± 0.2	0.095
End diastolic volume [mL]	113 ± 22	119 ± 35	0.212
End systolic volume [mL]	39 ± 14	48 ± 23	0.003
LV systolic function			
LV ejection fraction [%]	64 ± 7.7	60 ± 10	0.006
LV shortening fraction [%]	34 ± 5.1	32 ± 6.5	0.071
Stroke volume [mL]	72 ± 19	71 ± 19	0.809
Ejection time [ms]	315 ± 42	279 ± 42	< 0.001
Tei index	0.37 ± 0.2	0.36 ± 0.3	0.003
Lateral s' [cm/s]	7.1 ± 1.9	6.8 ± 1.8	0.468
Septal s' [cm/s]	6.1 ± 1.5	5.7 ± 1.5	0.142
Septal MAPSE [cm]	1.4 ± 0.3	1.3 ± 0.3	0.036
Lateral MAPSE [cm]	1.6 ± 0.3	1.5 ± 0.3	0.077
LV diastolic function			
IVRT [ms]	101 ± 28	127 ± 30	< 0.001
E wave [cm/s]	57 ± 14	56 ± 18	0.692
A wave [cm/s]	64 ± 16	72 ± 18	0.009
E/A ratio	0.9 ± 0.6	0.9 ± 0.7	0.783
EDT [ms]	174 ± 40	178 ± 50	0.545
Lateral e' [cm/s]	8.1 ± 2.9	7.8 ± 3.3	0.627
Lateral a' [cm/s]	9.2 ± 2.4	9.3 ± 2.9	0.730
E/e' ratio	8.3 ± 2.3	9.2 ± 3.9	0.092
Septal e' [cm/s]	6.5 ± 2.0	5.7 ± 2.0	0.017
Septal a' [cm/s]	7.9 ± 1.5	7.9 ± 2.5	0.921
LA dimension and function			
LA diameter [cm]	3.7 ± 0.3	3.9 ± 0.5	0.090
Maximal LA volume [mL]	52 ± 16	56 ± 22	0.213
Minimal LA volume [mL]	19 ± 8	23 ± 14	0.022
LA emptying fraction [%]	65 ± 8	60 ± 11	0.026
Aortic measurements			
Aorta [cm]	3.4 ± 0.3	3.4 ± 0.4	0.543
Ascending aorta [cm]	3.5 ± 0.3	3.6 ± 0.4	0.125

LV — left ventricular; LA — left atrium; MAPSE — mitral annular plane systolic excursion; IVRT — isovolumic relaxation time; RV — right ventricular; EDT — E wave deceleration time; A — atrial velocity; a' — late diastolic myocardial velocity; E — early mitral inflow velocity; e' — early diastolic myocardial velocity; s' — systolic myocardial velocity

Dialysis patients with LVH versus without LVH (Tables 3, 4)

In addition to the increased LVM and LVMI, the dialysis patients with LVH had lower weight, lower BSA, higher blood iron level, larger LV end

diastolic volume, higher LVEF and LV stroke volume ($p < 0.05$, for all) compared to dialysis patients without LVH. All the other clinical, biochemical and echocardiographic indices were not different between the two groups.

Table 3. Clinical, anthropometrical and biochemical data in study subjects.

Variable	Group 1 (n = 65)	Group 2 (n = 24)	Group 3 (n = 25)	Group 4 (n = 30)	P
Age [years]	56 ± 13	54 ± 13	59 ± 13	52 ± 13	0.186
SBP [mmHg]	155 ± 25	148 ± 21	146 ± 21	136 ± 18 ³	0.004
DBP [mmHg]	83 ± 14	81 ± 11	88 ± 10	86 ± 9	0.098
Heart rate [bpm]	80 ± 13	83 ± 12	78 ± 11	76 ± 9	< 0.001
Waist [cm]	87 ± 13	92 ± 10	95 ± 12 ²	97 ± 11 ^c	< 0.001
Hips [cm]	97 ± 12	103 ± 11	102 ± 12	107 ± 9 ^c	< 0.001
Waist/hips ratio	0.89 ± 0.06	0.89 ± 0.06	0.93 ± 0.06 ²	0.91 ± 0.07	0.030
Weight [kg]	64 ± 13	74 ± 13 ¹	73 ± 11 ²	85 ± 12 ^{c,5,6}	< 0.001
Body mass index [kg/m ²]	24 ± 5	25 ± 4	27 ± 3 ²	28 ± 3 ^c	< 0.001
Body surface area [m ²]	0.9 ± 0.2	1.0 ± 0.2 ¹	1.0 ± 0.18 ²	1.1 ± 0.18 ^{c,5,6}	< 0.001
Adiponectin [μg/mL]	16 ± 8.6	13 ± 8.9	6.8 ± 2.5 ^{b,4}	5.1 ± 2.8 ^{c,e}	< 0.001
C-reactive protein [mg/L]	12 ± 9	9 ± 4	4 ± 3	3 ± 2	0.037
HDL-cholesterol [mmol/L]	0.9 ± 0.2	1.0 ± 0.4	1.2 ± 0.6 ^b	0.8 ± 0.3 ^f	< 0.001
Total cholesterol [mmol/L]	4.5 ± 0.95	4.7 ± 0.97	4.7 ± 1.0	4.8 ± 0.65	0.294
Triglyceride [mmol/L]	1.8 ± 0.8	2.0 ± 0.8	1.5 ± 0.6	1.7 ± 0.4	0.108
Creatinine [μmol/L]	703 ± 170	733 ± 125	80 ± 18 ^{b,d}	79 ± 15 ^{c,e}	< 0.001
Blood urea nitrogen [mmol/L]	27 ± 6	27 ± 5	5.5 ± 1.7 ^{b,d}	5.3 ± 1.1 ^{c,e}	< 0.001
Total calcium [mmol/L]	2.1 ± 0.4	2.2 ± 0.2	2.2 ± 0.1	2.2 ± 0.2	0.698
Iron [μmol/L]	18 ± 9	13 ± 6 ¹	18 ± 3	20 ± 6 ⁵	0.005
Fasting glucose [mmol/L]	7.2 ± 4.0	6.2 ± 3.2	5.5 ± 0.6	5.7 ± 1.9	0.062
Albumin [g/L]	40 ± 4	40 ± 3	38 ± 2	37 ± 4 ³	0.003
Total proteins [g/L]	65 ± 5	64 ± 6	66 ± 2	66 ± 3	0.213
Aspartate aminotransferase [U/L]	22 ± 18	15 ± 5	18 ± 6	18 ± 5	0.169
Alanine aminotransferase [U/L]	26 ± 23	16 ± 9	19 ± 8	20 ± 8	0.078
Red blood cells [× 10 ⁶ /uL]	3.4 ± 0.7	3.6 ± 1.2	4.3 ± 0.6 ^{b,4}	4.7 ± 0.5 ^{c,e}	< 0.001
White blood cells [× 10 ³ /uL]	7.6 ± 3.7	7.0 ± 1.3	7.5 ± 1.3	7.8 ± 1.2	0.755
Hematocrit [%]	33 ± 5.5	32 ± 5.4	38 ± 4.2 ^{2,4}	40 ± 7.3 ^{c,e}	< 0.001
Hemoglobin [g/dL]	10 ± 1.7	10 ± 1.5	13 ± 1.6 ^{b,d}	14 ± 0.8 ^{c,e}	< 0.001

(1): p < 0.05 gr. 1 vs. gr. 2; (2): p < 0.05 gr. 1 vs. gr. 3; (3): p < 0.05 gr. 1 vs. gr. 4; (4): p < 0.05 gr. 2 vs. gr. 3; (5): p < 0.05 gr. 2 vs. gr. 4; (6): p < 0.05 gr. 3 vs. gr. 4
(a): p < 0.001 gr. 1 vs. gr. 2; (b): p < 0.001 gr. 1 vs. gr. 3; (c): p < 0.001 gr. 1 vs. gr. 4; (d) p < 0.001 gr. 2 vs. gr. 3; (e): p < 0.001 gr. 2 vs. gr. 4; (f): p < 0.001 gr. 3 vs. gr. 4
Gr. 1 — dialysis patients with LV hypertrophy; Gr. 2 — dialysis patients without LV hypertrophy; Gr. 3 — non-dialysis with LV hypertrophy; Gr. 4 — non-dialysis without LV hypertrophy
LV — left ventricular; SBP — systolic blood pressure; DBP — diastolic blood pressure; ACE — angiotensin converting enzyme; HDL — high-density lipoprotein

Dialysis patients with LVH versus non-dialysis patients with LVH (Tables 3, 4)

Dialysis patients with LVH, had higher adiponectin (Fig. 1), lower HDL-C, lower hemoglobin and RBC, shorter LVET (p < 0.001, for all), lower weight/hip ratio, lower BMI and BSA, lower hematocrit, lower baseline heart rate and broader QRS complex (p < 0.05 for all), compared to non-dialysis LVH patients. All other clinical, biochemical and echocardiographic indices did not differ between the two groups.

Relationship of adiponectin with clinical, biochemical and cardiac function indices in dialysis patients versus controls (Table 5)

In all study patients, adiponectin had strong correlation with LVMI (p < 0.001) (Fig. 2). In dialysis patients, adiponectin had a strong correlation with anthropometric parameters (waist measures, BMI and BSA, p < 0.001, for all) (Figs. 3, 4), good correlation with LVMI (p = 0.005) (Fig. 5), but weak correlation with waist/hips ratio (p = 0.037) and with total cholesterol level (p = 0.013). On the

Table 4. Echocardiographic data of study subjects.

Variable	Group 1 (n = 65)	Group 2 (n = 24)	Group 3 (n = 25)	Group 4 (n = 30)	P
LV dimension and mass					
LVM [g]	245 ± 66	190 ± 45 ¹	237 ± 100	196 ± 39 ³	< 0.001
LVMI [g/m ^{2.7}]	78 ± 27	41 ± 5 ^a	59 ± 10 ^{b,4}	38 ± 7 ^{c,f}	< 0.001
Interventricular septum [cm]	1.3 ± 0.25	1.1 ± 0.14	1.2 ± 0.17	1.1 ± 0.14 ³	< 0.001
LV posterior wall [cm]	1.1 ± 0.17	1.0 ± 0.13	1.0 ± 0.13	1.0 ± 0.14	0.039
End diastolic volume [mL]	125 ± 37	105 ± 26 ¹	115 ± 21	112 ± 23	0.032
End systolic volume [mL]	50 ± 24	44 ± 21	43 ± 144	35 ± 13 ³	0.016
LV systolic function					
LV ejection fraction [%]	61 ± 8	59 ± 12 ¹	62 ± 7	66 ± 8 ^{3,5}	0.012
LV shortening fraction [%]	33 ± 6	31 ± 8	33 ± 5	35 ± 5	0.099
Stroke volume [mL]	75 ± 19	61 ± 18 ¹	68 ± 22	74 ± 17	0.010
Filling time [ms]	391 ± 95	375 ± 74	434 ± 117	397 ± 80	0.144
Ejection time [ms]	278 ± 43	282 ± 40	324 ± 50 ^{b,4}	308 ± 33 ³	< 0.001
Tei index	0.39 ± 0.3	0.30 ± 0.2	0.34 ± 0.2	0.40 ± 0.2	0.396
t-IVT [ms]	7.8 ± 3.8	6.8 ± 3.3	6.6 ± 4	8.7 ± 4.5	0.162
Lateral s' [cm]	6.9 ± 1.9	6.7 ± 1.6	6.5 ± 1.7	7.5 ± 1.9	0.189
Septal s' [cm/s]	5.5 ± 1.4	6.5 ± 1.5	5.3 ± 1.0	6.8 ± 1.5	< 0.001
Septal MAPSE [cm]	1.3 ± 0.3	1.4 ± 0.3	1.4 ± 0.3	1.5 ± 0.3 ³	0.014
Lateral MAPSE [cm]	1.5 ± 0.3	1.6 ± 0.3	1.6 ± 0.3	1.6 ± 0.2	0.199
LV diastolic function					
IVRT [ms]	128 ± 32	127 ± 28	100 ± 29 ^{2,4}	102 ± 27 ^{6,5}	< 0.001
E wave [cm/s]	57 ± 20	53 ± 12	56 ± 13	58 ± 15 ³	0.734
A wave [cm/s]	73 ± 19	70 ± 14	68 ± 17	61 ± 15	0.021
E/A	0.9 ± 0.7	0.8 ± 0.3	0.8 ± 0.3	1.0 ± 0.7	0.729
EDT [ms]	185 ± 53	163 ± 38	176 ± 46	171 ± 34	0.241
Lateral e' [cm/s]	7.7 ± 3.2	8.2 ± 3.7	7.3 ± 2.2	8.7 ± 3.3	0.323
Lateral a' [cm/s]	9.1 ± 2.7	10 ± 3.2	9.1 ± 2.4	9.2 ± 2.4	0.458
Lateral s' [cm/s]	6.9 ± 1.9	6.7 ± 1.6	6.5 ± 1.7	7.5 ± 1.9	0.189
Septal e' [cm/s]					
Septal a' [cm/s]	8 ± 2.4	9 ± 2.6	8 ± 1.6	8 ± 1.3	0.182
Septal s' [cm/s]	6 ± 1.4	6 ± 1.5	5 ± 1.0 ⁴	7 ± 1.5 ^{c,f}	< 0.001
LA dimension and function					
LA diameter [cm]	3.9 ± 0.5	3.8 ± 0.5	3.7 ± 0.3	3.7 ± 0.3	0.383
LA maximal volume [mL]	52.5 ± 16	61 ± 28	56 ± 23	53 ± 20	0.558
LA minimal volume [mL]	19 ± 9	26 ± 17	23 ± 13	24 ± 15	0.353
LA emptying fraction [%]	65 ± 10	62 ± 11	61 ± 9	56 ± 13	0.080
Aortic measurement					
Aorta [cm]	3.6 ± 0.4	3.5 ± 0.4	3.4 ± 0.3	3.4 ± 0.3	0.704

(1): p < 0.05 gr. 1 vs. gr. 2; (2): p < 0.05 gr. 1 vs. gr. 3; (3): p < 0.05 gr. 1 vs. gr. 4; (4): p < 0.05 gr. 2 vs. gr. 3; (5): p < 0.05 gr. 2 vs. gr. 4; (6): p < 0.05 gr. 3 vs. gr. 4
(a): p < 0.001 gr. 1 vs. gr. 2; (b): p < 0.001 gr. 1 vs. gr. 3; (c): p < 0.001 gr. 1 vs. gr. 4; (d): p < 0.001 gr. 2 vs. gr. 3; (e): p < 0.001 gr. 2 vs. gr. 4; (f): p < 0.001 gr. 3 vs. gr. 4
Gr. 1 — hemodialysis with LV hypertrophy; Gr. 2 — emodialysis without LV hypertrophy; Gr. 3 — non hemodialysis with LV hypertrophy; Group 4 — non hemodialysis without LV hypertrophy
LV — left ventricular; LVM — left ventricular mass; LVMI — left ventricular mass index; LA — left atrium; RV — right ventricle; MAPSE — mitral annular plane systolic excursion; IVRT — isovolumic relaxation time; t-IVT — total isovolumic time; EDT — E wave deceleration time; A — atrial diastolic velocity; a' — late diastolic myocardial velocity; E — early mitral inflow velocity; e' — early diastolic myocardial velocity; s' — systolic myocardial velocity

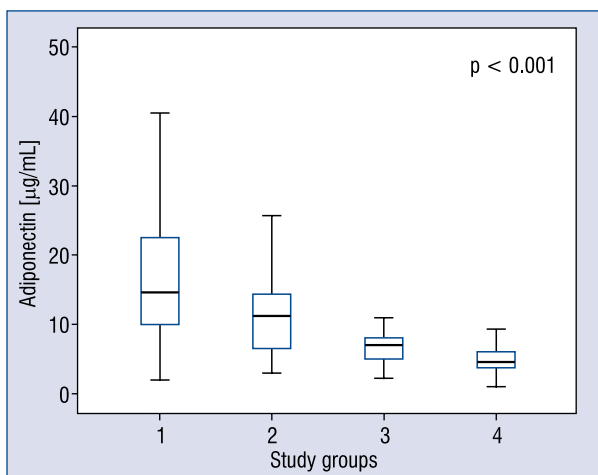


Figure 1. Adiponectin level in study groups of patients; 1 — Group 1 (dialysis patients with LVH); 2 — Group 2 (dialysis patients without LVH); 3 — Group 3 (non-dialysis patients with LVH); 4 — Group 4 (non-dialysis patients without LVH); LVH — left ventricular hypertrophy.

other hand, in controls, adiponectin only modestly correlated with age ($p = 0.024$), hemoglobin ($p = 0.005$), HDL-C ($p = 0.019$), and LVMI ($p = 0.043$) (Fig. 5), but no relationship was noted with the

other clinical, biochemical and echocardiographic parameters.

Discussion

The findings of this study can be summarized as follows: dialysis patients had lower BSA and BMI compared to age and gender matched controls but did have a larger LV cavity with thicker walls, higher LVMI and broader QRS duration. In addition, they were more anemic and had higher adiponectin levels compared to controls. Finally, while in dialysis patients adiponectin strongly correlated with BMI, it only modestly correlated with LVMI and volumes. The only relevant relationship in controls was with LVMI, although to a lesser strength than with dialysis patients.

Data interpretation. As expected, dialysis patients had lower body weight and BMI consistent with an element of cachexia, which is well known in patients with chronic kidney disease [39]. The profound degree of LVH resulting in higher mass index, again is consistent with the commonly found hypertension in this condition [40]. Such changes in LV structure resulted in significant functional disturbances in the form of reduced subendo-

Table 5. Correlation of adiponectin with clinical, biochemical and echocardiographic variables in study patients.

Variable	All study patients (n = 145)		Controls (n = 55)		Dialysis patients (n = 89)	
	r	p	r	p	r	p
Age	0.008	0.922	0.304	0.024	0.056	0.599
SBP	0.184	0.027	0.122	0.373	0.042	0.697
DBP	-0.099	0.238	0.075	0.586	-0.001	0.993
C-reactive protein	0.068	0.420	0.211	0.121	0.112	0.298
Cholesterol	-0.252	0.002	0.052	0.707	-0.292	0.013
HDL cholesterol	0.051	0.545	0.315	0.019	0.195	0.067
Hemoglobin	-0.427	< 0.001	0.371	0.005	-0.020	0.853
Urea	0.499	< 0.001	-0.153	0.266	-0.037	0.730
Creatinine	0.494	< 0.001	-0.084	0.544	-0.066	0.541
Waist	-0.461	< 0.001	-0.141	0.304	-0.427	< 0.001
Waist/hips ratio	-0.283	0.001	-0.184	0.178	-0.222	0.037
Body mass index	-0.468	< 0.001	-0.093	0.498	-0.403	< 0.001
Body surface area	-0.522	< 0.001	-0.096	0.487	-0.480	< 0.001
Left atrium	0.065	0.437	-0.075	0.585	0.001	0.996
Ejection fraction	-0.107	0.201	-0.162	0.237	0.044	0.684
Left ventricular mass	0.076	0.369	0.178	0.197	-0.013	0.904
LVMI	0.440	< 0.001	0.277	0.043	0.296	0.005

SBP — systolic blood pressure; DBP — diastolic blood pressure; HDL — high-density lipoprotein; LVMI — left ventricular mass index

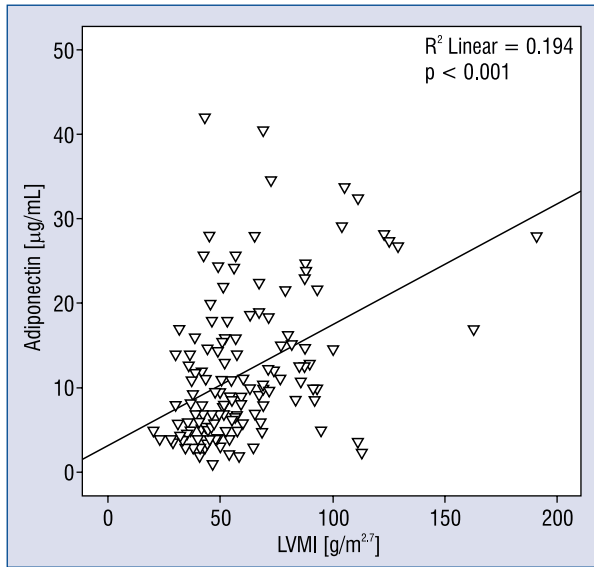


Figure 2. Correlation of adiponectin with left ventricular mass index (LVMI) in all study patients.

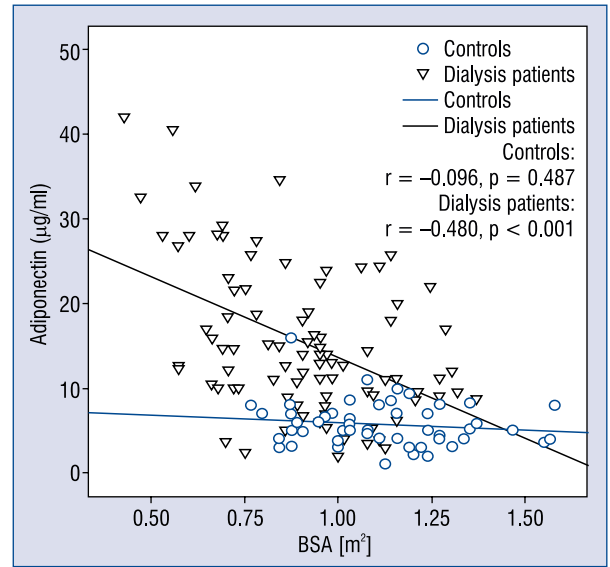


Figure 4. Correlation of adiponectin with body surface area (BSA) in dialysis patients and controls.

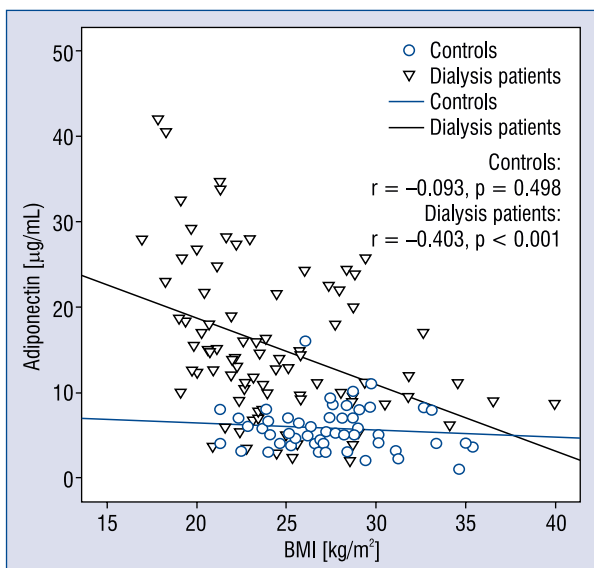


Figure 3. Correlation of adiponectin with body mass index (BMI) in dialysis patients and controls.

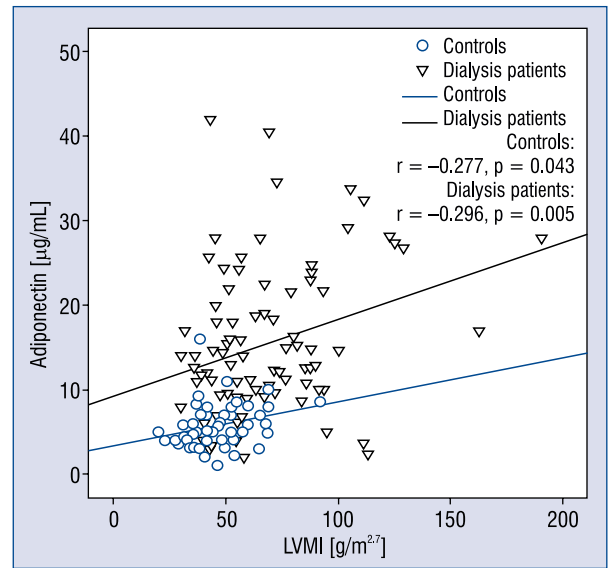


Figure 5. Correlation of adiponectin with left ventricular mass index (LVMI) in dialysis patients and controls.

cardial function reflected on the MAPSE and its myocardial velocities, enlargement of LV volume, lower ejection fraction and left atrial enlargement, typical to what is commonly seen in hypertensive LV disease without kidney failure [41]. Furthermore, the dialysis patients had some degree of dyssynchrony in the form of broader QRS, along with shorter ejection and filling times, caused by prolonged isovolumic times. The enlargement

of LV volume could be interpreted on the basis of volume overload because of dialysis. Despite all these changes in LV structure and function adiponectin did not seem to be related to any of them, except weakly with LVMI. Only few studies exist in the literature, that assessed a relationship between LVMI and adiponectin in dialysis patients. These studies include a small number of patients and their direct comparison with the present re-

sults has limitations. Komaba et al. [4] included only diabetic patients with dialysis, and Amira et al. [42] found good correlation, whereas Ayerden Ebinç et al. [23] was the only study whose results were in line with ours, having found a weak correlation between adiponectin and LVMI in dialysis patients. The strongest relationship found herein was between adiponectin and BMI, which is a reliable measure of body fat. These results support the close relationship of adiponectin and its site of secretion, i.e. the adipose tissue, rather than with cardiac structure and function.

Limitations of the study

As suggested above, the potential effect of volume overload during dialysis on the LV causing cavity enlargement, this might also have affected left atrial size and LV filling velocities and timing, hence the lack of a relationship with adiponectine. Right heart structure and function in this analysis was not included which might have shed some light on potential relationships, although they are also likely to be affected by loading conditions.

Conclusions

Although adiponectin is an established cardio-protective marker, it does not seem to be related to cardiac structure and function parameters but only strongly to BMI suggesting an ongoing catabolic process associating dialysis.

Conflict of interest: None declared

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