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Original article

Association of overhydration and cardiac dysfunction in patients have chronic kidney disease but not yet dialysis

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ABSTRACT

Background/Aim. – Fluid overload and cardiac dysfunction is well established in hemodialysis patients. But in predialysis chronic kidney disease, the association of fluid overload and cardiac dysfunction is relatively unknown. In this study, we aimed to investigate the relationship between fluid overload and cardiac dysfunction in predialysis chronic kidney disease patients.

Method. – We enrolled 107 consecutive patients in our study. Fluid overload was assessed via body composition monitor. Patients were dichotomized according to the fluid overload status. The patients with FO < 1.1 L were determined as normovolemic and those with FO ≥ 1.1 L as hypervolemic according to the previously reported physiologic model. Left atrial volume index (LAVI), left ventricular end-diastolic–end-systolic index (LVEDVI, LVESVI), E/e', LVMI and global longitudinal left ventricular left ventricular strain (GLS-%) were evaluated in each patient as markers of cardiac dysfunction. Arterial stiffness was also assessed by Mobil-O-Graph® 24 h pulse wave analysis monitor and pWV values were recorded.

Results. – Fifty-five patients were normovolemic and 52 patients were hypervolemic. LAVI, LVMI, LDEDVI, LVEDSVI, E/e' were increased in hypervolemic patients. Also in hypervolemic patients pulse wave velocity was increased and GLS was decreased. Multivariate analysis showed that FO was independently associated with GLS which is the most specific echo-parameter for left ventricular dysfunction.

Conclusion. – FO was independently associated with cardiac dysfunction in patients with chronic kidney disease not ongoing dialysis. Effective treatment of hypervolemia may be important in these patients to avoid further cardiac damage.

1. Introduction

Hypervolemia/volume overload, apart from hypertension, age and atherosclerosis, may be another cause of cardiac injury in patients with chronic kidney failure [1]. Volume overload increases circulating volume, venous return and filling pressures. The result is myocardial systolic and diastolic stress. The effect of volume overload on systolic and diastolic functions of left ventricle had been investigated through several echocardiographic parameters.

The effect of FO on mitral inflow and pulmonary vein Doppler velocities had also been proven in previous studies [2]. Some other studies demonstrated the association between FO and left ventricular mass and also pulse wave velocity [3]. However, up to now there is no study investigating the association between FO and myocardial strain. In general, parameters of myocardial strain have been used to detect subclinical myocardial disease [4]. The myocardial involvement in cardiorenal syndrome and its association with fluid overload had never been studied in terms of myocardial strain before.

In patients with chronic kidney failure, mortality is correlated with the left ventricular mass index (LVMI) [5]. Quantification of fluid overload and its optimal management through bioimpedance method may reduce left ventricular hypertrophy and so the mortality in chronic kidney disease patients [6].

The aim of our study was to investigate the association between global left ventricular longitudinal strain (GLS) (a parameter which while showing subtle systolic dysfunction is independent from the

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parameters showing diastolic dysfunction) and FO in patients with chronic kidney failure (eGFR < 60 mL/min/1.73 m^2) who weren't undergoing dialysis.

2. Methods

2.1. Patient selection

This observational study was conducted at Antalya education and research hospital. This study was approved by the Institutional review board at Antalya education and research hospital. Exclusion criteria were as follows: any diagnosed acute or chronic inflammatory state within 3 months, hospitalization related dialysis within 3 months, diseases that produce local fluid accumulation and edema, active malignancy, currently taking diuretics, currently taking any medication with the potential to influence body composition, malnutrition, pregnancy, insertion of a cardiac pacemaker or defibrillator, or the amputation of any extremity. All of the patients provided informed consent. eGFR was calculated using the 4-variable MDRD Study equation [7].

2.2. Body composition and fluid overload analysis

A body composition monitor (BCM) (Fresenius Medical Care, Bad Homburg, Germany) was used to determine the extracellular and total body water. FO was calculated using a physiological BCM model that is based on tissue properties [8]. In the light of the physiological data reported by Moissl et al., 1.1 L was accepted as cut-off value for FO [9]. The BCM measures the impedance spectroscopy at 50 different frequencies between 5 kHz and 1 MHz. Electrodes were attached to one hand and one foot at the ipsilateral side, after the patient had been in recumbent position for at least 5 minutes. For determination of weight, we used the weight measured in morning and in fasting state. FO were determined from the measured impedance data following the model of Moissl et al. [9].

2.3. Assessment of pulse wave velocity

Mobil-O-Graph® 24 hour pulse wave analysis monitor (I.E.M. Industrielle Entwicklung Medizintechnik und Vertriebsgesellschaft mbH Cockerillstraße Stolberg (Rheinland), Germany) was used for the measurements of arterial stiffness and central blood pressure analysis [10]. Built-in combining algorithms in the device were used for central aortic and brachial blood pressure measurements and PWV analysis. Assessment of pulsatile hemodynamics: PWV was determined as a measure of arterial stiffness. Also central blood pressure data were obtained with pulse wave analysis monitor.

2.4. Echocardiography

Echocardiography was performed with synchronized electrocardiography with a commercially available system (Philips iE33, Bothell, WA, USA) equipped with a broadband S5-1 transducer The Automated Function Imaging algorithm allowed GLS. Ts-SD was automatically calculated by echo system from longitudinal strain using time-to peak variation, defined as the standard-deviation of time-to-peak over all 17 segments. LVMI was calculated, according to the method of Devereux [11]. LAVI was calculated by automatic algorithm based on the modified Simpson's method built on the device [12]. LVEDVI and LVESVI along with the LVEF were calculated by the biplane Simpson's method from apical 4-chamber views Tissue Doppler-derived early (e'), and early diastolic (E) velocities were derived from the septal mitral annulus.

2.5. Statistical analysis

Data were analyzed utilizing the SPSS software version 17.0 for Windows (SPSS Inc., Chicago, IL, USA). Whether the data is normal distribution or not, were analyzed with Kolmogorow Smirnov and Shapiro Wilk test. Data with normal distribution were presented as mean ± SD, non-normally distributed data were presented as median [max–min]. Continuous variables without normal distribution were analyzed using Mann-Whitney U test. Normal distribution data were compared by Student *t* test. In the analysis of categorical data, chi-square and Fisher's exact tests were used. The association pf different variables with FO and GLS were calculated by univariate analysis for each. The variables for which the unadjusted P value was <0.05 in univariate analysis were included in the multivariable Cox regression model. A *p* value <0.05 was considered to be statistically significant.

3. Results

By using 1.1 as a cut-off point, the patients were divided in two groups according to their FO state [9]. In the overhydrated group albumin and hemoglobin values were significantly lower (respectively $P = 0.03$ and $P = 0.01$). Diabetes (DM) were more frequent (31% vs. 18%; $P = 0.05$) in the overhydrated group and the central systolic blood pressure ($P = 0.008$) and pulse wave velocity ($P = 0.02$) were also significantly higher in this group. There was no significant difference between the groups in respect of the medications they were using (Table 1).

When assessed in combination with data form conventional echocardiography, GLS ($P < 0.001$), was significantly lower whereas ts-SD ($P = 0.007$) and LVMI ($P < 0.001$) values were significantly higher in the overhydrated group. The values of LVEDVI ($P = 0.02$), LVESVI ($P = 0.09$), E/e' ($P = 0.02$) and LAVI ($P = 0.001$) were also found to be higher in the overhydrated group. There was no significant difference between the groups in respect of EF (Table 2).

In the univariate analysis, a relationship was found between fluid overload and DM (β = 3.157; 95% CI [1.395–7.496]; $P = 0.06$), PWv (β = 1.309; 95% CI [1.050–1.631]; $P = 0.016$), systolic blood pressure (β = 1.027; 95% CI [1.007–1.047]; $P = 0.07$), pulse pressure (β = 1.036; 95% CI [1.009–1.063]; $P = 0.008$), mean arterial pressure (β = 1.034; 95% CI [1.006–1.064]; $P = 0.018$), central systolic blood pressure (β = 1.037; 95% CI [1.007–1.0053]; $P = 0.011$), serum albumin levels (β = 0.245; 95% CI [0.065–0.925]; $P = 0.038$) and hemoglobin levels (β = 0.720; 95% CI [0.555–0.935]; $P = 0.014$). However, no relation was detected between FO and age, gender, parathormone (PTH) levels and eGFR. Multivariate logistic regression analysis showed an independent association between overhydration and DM (β = 1.221; 95% CI [1.268–9.064]; $P = 0.015$] and also hemoglobin levels (β = −0.472; 95% CI [0.442–0.879]).

During the echocardiographic analysis, the GLS values were found to be lower in the overhydrated group while the EDVI, ESVI, ts-SD, LVMI, LAVI and E/e' values were found to be higher (Table 2).

A univariate regression analysis was performed between the GLS and clinical and laboratory parameters. According this analysis FO, diabetes, age, gender, PWv and PTH were found to be significantly associated with GLS. However eGFR, blood pressure and hemoglobin levels were not associated with GLS. On multivariate analysis FO and PTH levels were found as the independent associates of GLS (Table 3 and Fig. 1).

4. Discussion

In patients who do not undergo dialysis, a decrease in GFR is associated with an increase in cardiovascular events [13]. As the majority of these patients have severe cardiac risk factors such as