Differences in Cardiac Structure Assessed by Echocardiography Between Renal Transplant Recipients and Chronic Kidney Disease Patients

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ABSTRACT

Background. Cardiovascular disease (CVD) is the leading cause of death in predialysis chronic kidney disease (CKD) and dialysis patients as well as in renal transplant recipients (RTRs). Left ventricular hypertrophy (LVH) starts early during the course of CKD and is a strong predictor of CVD in this population. Regression of LVH after a successful renal transplantation remains a debatable issue among investigators, whereas there is little data comparing echocardiographic measurements between patients with predialysis CKD and RTRs.

Aim. The aim of this study was to compare echocardiographic measurements of LV structure and function between predialysis CKD patients and RTRs of similar renal function level.

Patients and Methods. We conducted a case control study with individual (1:2) matching from the Renal Transplant and the predialysis CKD Outpatient Clinic. For each of the 36 RTRs, two matched for gender, age and estimated glomerular filtration rate (eGFR) predialysis CKD outpatients (72 patients) were included. All patients underwent transthoracic echocardiography and LV mass, LV mass index [LVM and LVMI = LVM/BSA g/m^2] and indices of systolic function were measured. In a subgroup of 12 RTRs we retrospectively assessed and compared the LVMI measurements at three different time points, during predialysis, dialysis and post transplant period.

Results. The prevalence of LVH was 33% in RTRs and 52% in CKD patients (ns). RTRs had significantly lower LVM and LVMI levels compared with predialysis CKD patients ($P = .006$ and $P = .008$) while the other echocardiographic indices did not differ. In the subgroup of 12 RTRs, post-transplant LVMI levels (105 ± 25 g/m^2) were significantly lower in comparison with predialysis (147 ± 57 g/m^2) and dialysis LVMI levels (169 ± 72 g/m^2) ($P = .01$, $P = .01$, respectively).

Conclusion. RTRs had significantly lower LVMI compared with predialysis CKD patients of similar age, renal function, hemoglobin and blood pressure level.

CARDIOVASCULAR DISEASE (CVD) is a major cause of death in predialysis and dialysis patients as well as in renal transplant recipients (RTRs) [1]. Change in left ventricular (LV) structure in the form of left ventricular hypertrophy (LVH) is a common co-morbidity in chronic kidney disease (CKD) [2] and an established, strong risk factor for CVD in this population [3]. LVH starts early in the course of CKD and is inversely correlated with renal function [2]. In end stage renal disease (ESRD), 75% of patients have LVH at the start of dialysis due mainly to hypertension, volume expansion and anemia [4]. In a

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number of studies a successful renal transplantation has been associated with significant echocardiographic regression of LVH in RTRs [5–8], while others studies have shown no positive effect [9,10]. The expansion and variation of intravascular volume in dialysis patients compared with RTRs has been suggested as one of the reasons for the contradictory results [10]. The comparison of the echocardiographic LV measurements between predialysis CKD patients and RTRs with similar renal function constitutes probably an alternative way to approach this debatable issue, to assess indirectly the effect of renal replacement treatment on LV mass (LVM) and moreover to investigate the difference of LVH severity between these two patients' groups.

The aim of this study was to compare echocardiographic indices of LV structure between age-matched predialysis CKD patients and RTRs of similar renal function. Secondly, in a subgroup of RTRs, the possible LVM changes from the predialysis CKD period until the post-transplant phase were also assessed.

PATIENTS AND METHODS

Patients

In this case control study we included 36 RTRs from the Renal Transplant Outpatient Clinic of the University Hospital of Ioannina in North Western Greece. For each of the 36 RTRs, two predialysis CKD outpatients matched for gender, age and estimated glomerular filtration rate (eGFR) were recruited. Exclusion criteria for all patients were any CV event (defined as stroke, peripheral vascular disease, myocardial infarction and acute ischemic heart disease) occurring within a period of 3 months prior to study entry, heart failure NYHA stage IV, any moderate or severe valvular heart disease, presence of clinical infection and active malignancy. Moreover, in a subgroup of twelve RTRs the LVM index (LVMI) measurements were retrospectively assessed at two different time points, the first during the predialysis period and the second during dialysis treatment and compared with the LVMI estimation during the post-transplant period. All RTRs had a functioning allograft for at least six months and were receiving a calcineurin inhibitor-based (tacrolimus or cyclosporine) immunosuppression. The study was approved by the local hospital Ethical Committee and patients participated in the study after providing informed consent.

Methods

At study entry all patients underwent a detailed review of their medical history and careful clinical examination. Additionally, demographic characteristics, co-morbidities (cardiovascular disease, diabetes mellitus, hypertension), medication and blood pressure (BP) were assessed. Hypertension was defined as systolic BP $\geq$140 mm Hg and/or diastolic BP $\geq$90 mm Hg, or current use of antihypertensive medication. A full hematological and biochemical screen was performed, urine protein (UPR) was measured in a 24 hour urine collection and eGFR (mL/min/1.73 m^2) was calculated by the CKD-EPI formula [11].

The transthoracic echocardiographic study (2D, M-mode and Doppler for assessment of valvular function) was performed usually within one week and no longer than 1 month from study entry, by an experienced echocardiographer, who was unaware of the clinical data and followed a predefined protocol for the recordings and measurements [12]. Left ventricular end-diastolic diameter (LVEDD), interventricular septum (IVS) and posterior wall (PW) thickness were measured according to standard convention [13]. LVM in grams was estimated with the Devereux formula [LVM = 1.04 $\times$ [(LVEDD + PW + IVS)^3 − LVEDD^3] − 13.6 g] [14]. LVMI was calculated by dividing LVM with the patient's body surface area [LVMI = LVmass (g)/BSA (m^2)]. LVH was defined LVMI >110 g/m^2 in females and LVMI >134 g/m^2 in males [15]. LV systolic function was assessed by the fractional shortening (FS) and ejection fraction (EF) according to standard recommendations [16]. FS was computed from linear measures of diastolic and systolic cavity sizes and wall thickness according to a standard formula [16] while EF was calculated using the biplane method of disks (modified Simpson's rule) [16].

Statistical Analysis

Data were presented as mean and standard deviation (for normally distributed data), median and interquartile range (for not-normally distributed data), or as absolute count and frequency in percent (for binary variables). Chi-square or Fisher Exact Test was used for categorical variables, whereas comparisons of continuous variables among the two groups of patients were analyzed using Student's *t*-test. Correlations were determined with Pearson's correlation coefficient. Multivariate linear regression analysis (backward method) was performed to determine the factors that were independently associated with LVMI levels in both groups of patients. Multivariate analysis in each group included all associations with a P value $\leq$ .2 in univariate analysis. A P value less than .05 was considered statistically significant. All analyses were performed by using SPSS 17.0 (SPSS, Chicago, IL).

RESULTS

Patient Baseline Characteristics

The baseline characteristics of the 36 RTRs (group 1) and 72 CKD patients (group 2) are summarized in Table 1. According to study design, the two patient groups were matched for age, gender and eGFR. There were no differences in co-morbidities (hypertension, diabetes mellitus and CVD), systolic and diastolic BP levels between the two groups (Table 1).

Regarding laboratory parameters, there were no significant differences in levels of hemoglobin (Hb), serum total cholesterol, LDL cholesterol, triglycerides, phosphorus, parathormone (PTH) and CRP between the study groups. Twenty four hours UPR content was significantly lower in the RTR group (P = .002) and serum calcium was significantly higher compared to the CKD group, as expected (P = .001) (Table 1).

With regards to medication, a significant higher percentage of RTRs were receiving β-blockers, vitamin-D, statins and erythropoietin compared to the CKD group (P < .001, P < .001, P = .03 and P = .035 respectively).

Echocardiographic Measurements

The echocardiographic findings of the two groups are shown in Table 2. There were no significant differences in levels of EF or FS between the two groups of patients. The prevalence of LVH was lower in RTRs (33%) than in CKD patients (52%), but the difference was not statistically significant.