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Assessment of cardiovascular risk in paediatric peritoneal dialysis patients: a Turkish Pediatric Peritoneal Dialysis Study Group (TUPEPD) report

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Abstract

Methods. We aimed to clarify arteriosclerotic risk and to document possible relationships between cardiovascular risk factors and echocardiographic parameters in paediatric peritoneal dialysis (PD) patients. M-mode/Doppler/tissue Doppler echocardiographic studies and lipid/lipoproteins, homocysteine, high-sensitivity C-reactive protein (HS-CRP) levels and carotid intima–media thickness (CIMT) were determined in 59 patients (age: 14.2 ± 4.5 years) and in 36 healthy subjects.

Results. Structural and functional cardiac abnormalities were observed in patients on maintenance dialysis. Increased left ventricular mass index (LVMI, $P = 0.000$), relative wall thickness ($P = 0.000$), myocardial performance index (MPI, $P = 0.000$) were documented in the patients. Lipoprotein (a) ($P = 0.000$), homocysteine ($P = 0.001$), HS-CRP ($P = 0.000$) and CIMT ($P = 0.000$) were significantly elevated in the patients. Left ventricular hypertrophy (LVH) was prevalent in 68% of the patients. Patients with LVH had higher levels of HS-CRP ($P = 0.001$) and CIMT ($P = 0.028$) than those without LVH. Haemoglobin was an independent predictor of LVMI (β: −8.9, $P = 0.001$), while residual diuresis and CIMT were independent predictors of diastolic dysfunction (β: −0.45, $P = 0.034$ and β: 5.90, $P = 0.008$, respectively). Albumin (β: −0.72, $P = 0.018$) and Kt/V urea (β: −0.48, $P = 0.012$) were significant predictors of CIMT. There were positive correlations between LVMI and CIMT. HS-CRP was positively correlated with LVMI as well as CIMT.

Conclusions. Elevated levels of atherosclerotic/inflammatory risk factors, low haemoglobin levels and loss of residual renal function and their negative effects on heart are of remarkable importance in paediatric patients on maintenance peritoneal dialysis. Achieving recommended targets for haemoglobin, blood pressure and Kt/V urea, preserving residual renal function as well as

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managing inflammation and subsequent arteriosclerosis is obviously essential to improve the patients' prognosis.

Keywords: cardiovascular disease; children; chronic kidney disease; echocardiography; peritoneal dialysis

Introduction

Compared to the general paediatric population, children with end-stage renal disease (ESRD) have an increased risk for death, particularly from cardiovascular disease (CVD) due to the development of accelerated arteriosclerosis and premature cardiomyopathy [1–4]. Cardiovascular (CV) causes accounted for 41% of all deaths in children with ESRD in the paediatric Dutch study and for 21.3% in the recent NAPRTCS report [2,5]. The annual report of USRDS indicated that [6] CV mortality among children with dialysis rose from 17.7 deaths/1000 patient-years in 1991 to 23.4 in 2005, which points out the emerging importance of CVD in uraemic children. Although, this particular preponderance has traditionally been associated with numerous traditional CV risk factors, much recent interest has focused on non-traditional risk factors such as inflammation and endothelial dysfunction [1,7,8]. Increased carotid artery intima–media thickness (CIMT), one of the first signs of early atherosclerosis, is introduced by high blood pressure (BP), dyslipidaemia, hyperhomocysteinaemia and microinflammation [9,10]. Elevated serum concentrations of C-reactive protein (CRP) is another marker used to stratify CV risk by reflecting chronic inflammation in adult and paediatric chronic kidney disease (CKD) and dialysis patients [11–14]. High-sensitivity CRP (HS-CRP) has recently emerged as a useful biomarker for vascular inflammation associated with atherosclerosis. Determination of HS-CRP levels is currently recommended by the American Heart Association (AHA) in all patients at a risk of CVD [15]. Both CIMT and HS-CRP have been shown to be elevated in paediatric dialysis patients in a recent study [16].

Cardiac structural and functional abnormalities are highly prevalent in paediatric ESRD patients and contribute to morbidity [1,3,4,8]. Left ventricular hypertrophy (LVH) is an independent risk factor involved in the development of CVD in paediatric dialysis patients [1,8]. Systolic and diastolic dysfunction have also been demonstrated in paediatric studies [17,18]. Recently, new indices were introduced to evaluate diastolic function using tissue Doppler imaging (TDI) that provides a more accurate measurement. Recent studies employing TDI determined that children on peritoneal dialysis (PD) have abnormal diastolic function [19,20].

In this report, we aimed to evaluate arteriosclerotic risk factors and early markers of inflammation including serum lipid/lipoprotein fractions, apolipoprotein B, homocysteine, HS-CRP and CIMT and to document possible relationships between those markers and echocardiographic parameters by M-mode, pulsed wave Doppler (PWD) and TDI in paediatric PD patients as a report of Turkish Pediatric Peritoneal Dialysis Study Group (TUPEPD).

Patients and methods

Fifty-nine patients aged 14.2 ± 4.5 (range: 6.25–24.2) years and treated with PD for a period of 39 ± 31 (3–108) months in nine paediatric PD centres and 36 age-, gender- and body mass index (BMI)-matched healthy subjects (mean age 12.9 ± 1.9) as a control group were enrolled in this study. The patients on PD <3 months and having an acute infection during the last 3 months were excluded from the study.

Routine biochemical parameters, complete blood count, serum ferritin, parathormone (PTH) as well as HS-CRP levels were studied in patients on maintenance dialysis. CIMT was also measured in the patient group using a GE Logic 9 (Milwaukee, WI) ultrasound system and a 10-MHz probe in each centre as previously described [57]. Detailed echocardiographic examinations were done in both groups. Conventional and TDI echocardiography (Vivid 7 Pro, GE Medical Systems, Vingmed Ultrasound AS, N-3190 Horten, Norway) were performed by experienced paediatric cardiologists in each centre by following the same protocol. Echocardiography was performed after an overnight exchange for APD and after a manual early morning exchange for CAPD patients (fill volume of 1000–1100 ml/m^2) with a dry abdomen.

Left ventricular end systolic (LVES) and end diastolic diameters (LVED), interventricular and posterior wall thicknesses in systole and in diastole (IVES, IVED, PWES, PVED, respectively) were measured. Ejection fraction (EF), fractional shortening (FS) and meridional wall stress (WS) were calculated based on the American Society of Echocardiography guidelines for assessing systolic function (WS: $0.98 \times (0.334 \times \text{SBP} \times \text{LVES})/[\text{PWES} \times (1 + (\text{PWES}/\text{LVES}))] - 2$ ($\times$103 dynes/cm^2) [58]. LVM was calculated using the Devereux formula [59], and LVM index (LVMI; mass divided by height raised to a power of 2.7, g/m$^{2.7}$) was used to evaluate LVH [60]. LVH was defined as LVMI greater than the 95th percentile for normal children and adolescents [61]. The relative wall thickness (RWT) was calculated as an index of the LV geometric pattern: RWT = (IVED + PWED)/LVED. Concentric LVH was defined as increased LVMI and RWT greater than the 95th percentile of paediatric patients; eccentric LVH was defined as elevated LVMI with normal RWT, and concentric remodelling was defined as normal LVMI but elevated RWT [62]. PWD echocardiography was used to evaluate transmitral LV filling velocities at the tips of the mitral valve leaflets. Peak flow velocities for LV inflow in early diastole (E) and late diastole during atrial contraction (A) were measured. An E/A ratio, deceleration time (DT) and isovolumic relaxation time (IVRT) were recorded. Pulsed-TDI was assessed during both contraction and relaxation of LV to assess sample velocity at the lateral margins of mitral annulus. Early (TDI E) and late (TDI A) diastolic velocities were recorded. The PWD E/TDI E ratio was calculated as a reliable measure of diastolic function [36]. The myocardial performance index (MPI) reflecting combined systolic/diastolic dysfunction was calculated as previously described by [63]. All parameters were measured during three consecutive cardiac cycles, and their mean value was calculated.

Statistical analysis

Categorical variables were analysed by the chi-square test. Differences between the two groups for continuous variables were evaluated by using Student's *t*-test or the Mann–Whitney *U*-test, where applicable. Correlations between variables were evaluated by using Pearson's and Spearman's correlation analyses, where applicable. Regression analysis was performed to determine the variables that significantly affect LVMI, PWD E/TDI E ratio as a measure of diastolic dysfunction and CIMT. Data were expressed as mean ± SD. *P*-values <0.05 were considered significant. SPSS version 13.0 was used (SPSS, Chicago, IL, USA). Local ethical committee approval was obtained.

Results

Etiologic causes of ESRD and descriptive features of the patients

There were 31 APD and 28 CAPD patients. The causes of ESRD are shown in Table 1. A total 39% ($n = 23$) of the patients had urological problems/tubulointerstitial diseases. The second most common group was primary glomeru-

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Table 1. Primary etiologic cause of end-stage renal disease in CPD patients

Diagnosis	*n*
Urological problems/tubulointerstitial diseases	
Vesicoureteral reflux	10
Posterior urethral valve	3
Neuropathic bladder	5
Chronic pyelonephritis	3
Tubulointerstitial nephritis	2
Primary glomerulonephritis	
Focal segmental glomerulosclerosis	5
Membranoproliferative glomerulonephritis	2
Crescentic glomerulonephritis	2
Congenital nephrotic syndrome	1
Hereditary/metabolic diseases	
FMF-amiloidosis	3
Cystinosis	2
Primary hyperoxaluria type 1	1
Galactosialidosis	1
Cystic renal diseases	
Autosomal recessive polycystic kidney disease	3
Juvenile nephronophthisis	3
Renal hypoplasia/dysplasia	6
Unknown aetiology	4
Miscellaneous	3
Total	59

Table 2. Somatometric data and BP levels of the patients and controls

	CPD (mean ± SD)	Control (mean ± SD)	*P*-value
Sex	Male ($n = 29$), female ($n = 30$)	Male ($n = 17$), female ($n = 13$)	0.378
Age (years)	14.2 ± 4.5	12.9 ± 1.9	0.102
Body weight (kg)	34.2 ± 14.7	46.5 ± 14.4	0.038
Height (cm)	134 ± 20	155 ± 14	0.002
Height SDS	−3.1 ± 1.4	0.1 ± 0.9	0.000
Body mass index (kg/m^2)	18.4 ± 4.5	20.1 ± 3.6	0.160
Body mass index SDS[a]	−0.3 ± 1.2	0.1 ± 0.9	0.006
Systolic BP (mmHg)	119 ± 17	111 ± 18	0.000
Diastolic BP (mmHg)	71 ± 14	61 ± 7	0.000

[a]Standard deviation score.

lonephritides (17%), as was reported in our national registry [21]. There were no diabetic patients. No patients had had a previous transplant, and none of the patients were on steroids or other immunosuppressives. Sixteen patients were anuric, 2 polyuric (urine output > 4 ml/kg/h), 12 oliguric (urine output < 0.5 ml/kg/h) and the remainder had some residual diuresis (urine output range >0.5 to <4 ml/kg/h). None of the patients had serum albumin levels <2.5 g/dl. Twenty-one patients (42%) were on antihypertensive medication (16 out of 21 patients were on a single drug, and 15 of 21 patients were on angiotensin-converting enzyme inhibitors) and 14 patients on lipid-lowering drugs.

Body weight and height were significantly lower in CPD patients compared to the controls, despite comparable age, BMI and sex distribution (Table 2). Systolic/diastolic BP levels were within the normal limits in 33 patients compared to the BP nomograms of the healthy Turkish paediatric population [22], 7 of whom were on anti-hypertensive medication. Twenty-six patients had uncontrolled hypertension, 14 of whom were on antihypertensive medications.

Table 3. Biochemical data of the patients

	Mean ± SD
Duration of peritoneal dialysis (months)	39 ± 31 (range 3–108)
Blood urea nitrogen (mg/dl)	53 ± 20
Creatinine (mg/dl)	7.9 ± 2.3
Uric acid (mg/dl)	5.6 ± 1.1
Albumin (g/dl)	3.5 ± 0.6
Triglyceride (mg/dl)	151 ± 82
Cholesterol (mg/dl)	193 ± 44
High-density lipoprotein cholesterol (mg/dl)	48 ± 15
Low-density lipoprotein cholesterol (mg/dl)	115 ± 36
Very low-density lipoprotein cholesterol (mg/dl)	30 ± 16
Calcium (mg/dl)	9.2 ± 1.0
Phosphorus (mg/dl)	5.4 ± 1.4
Ca × P product (mg^2/dl^2)	50 ± 14
Alkaline phosphatase (U/l)	458 ± 80 (mean ± SEM)
Parathormone (pg/ml) (N:12–72)	454 ± 62 (mean ± SEM)
Haemoglobin (g/dl)	9.9 ± 1.8
Ferritin (ng/ml)	374 ± 40 (mean ± SEM)
Erythrocyte sedimentation rate (mm/h)	62 ± 28
Creatinine clearance (ml/min/1.73 m^2)	9 ± 3
Weekly Kt/V urea	2.57 ± 0.95
Ultrafiltration volume (ml/day)	591 ± 64 (mean ± SEM)
Residual urine volume (ml/day)	882 ± 156 (mean ± SEM)

SD, standard deviation; SEM, standard error of the mean.

Laboratory data and atherosclerotic/inflammatory markers of the patients (Tables 3 and 4)

Lipid profile, uric acid levels and calcium–phosphorus product were found to be in acceptable limits; however, the

Table 4. Cardiovascular risk markers in the patients

	Patients (mean ± SD)	Controls (mean ± SD)	*P*-value
Apolipoprotein B (mg/dl)	105 ± 38	76.5 ± 20.6	0.002
Lipoprotein (a) mg/dl	39.9 ± 59.4 (median: 20.8)	15.5 ± 16.9 (median: 6.0)	0.000
Homocysteine (μm/l)	18.6 ± 15.0	10.3 ± 5.5	0.001
High-sensitivity C-reactive protein (mg/l) (N:0–0.3)	1.80 ± 3.20 (median: 0.56)	0.12 ± 0.04	0.000
Intima–media thickness of common carotid artery (mm)	0.62 ± 0.13	0.51 ± 0.10	0.000

SD, standard deviation.

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Table 5. Frequencies of cardiovascular risk factors in the patients

	N	%
Uncontrolled blood pressure[a]	**26**	**44**
With medication	14	24
Without medication	12	20
Controlled blood pressure	**33**	**56**
With medication	7	12
Without medication	26	44
Anaemia (<11 g/dl)	40	68
Dyslipidaemia[b]	23	39
Serum albumin (2.5–3.5 g/dl)	26	44
High Ca × P product	20	34
High HS-CRP	39	66
Obesity	5	8
Under-nutrition	4	7
Diabetes	0	
Smoking	0	

[a]Blood pressure >95th percentile.
[b]LDL-cholesterol >130 mg/dl or triglyceride >200 mg/dl + non-HDL-cholesterol >160 mg/dl.
K/DOQI Clinical Practice Guidelines for Managing Dyslipidaemias in Chronic Kidney Disease.

Table 6. Echocardiographic findings of the patients

	Patients (mean ± SD)	Controls (mean ± SD)	*P*-value
EF (%)	66 ± 12	73 ± 8	0.004
FS (%)	37 ± 7	37 ± 6	0.759
WS (g/cm^2)	49 ± 20	44 ± 11	0.114
RWT (cm)	0.55 ± 0.48	0.40 ± 0.09	0.000
LVMI/boy$^{2.7}$ (g/m^2)	61 ± 28	35 ± 10	0.000
PWD E/A ratio	1.5 ± 0.3	1.8 ± 0.5	0.000
IVRT (ms)	91 ± 18	78 ± 15	0.000
DT (ms)	166 ± 46	210 ± 45	0.000
MPI	0.70 ± 0.27	0.42 ± 0.07	0.000
TDI E/A ratio	1.85 ± 0.52	2.41 ± 0.87	0.000
PWD E/TDI E ratio	8.3 ± 3.4	6.5 ± 1.8	0.004

SD, standard deviation.

patients were moderately anaemic and had elevated HS-CRP levels. The parathormone (PTH) level was high. Kt/V urea levels were in acceptable limits (Table 3). Apolipoprotein B, lipoprotein (a), plasma homocysteine levels were all significantly higher in the patient group compared to those in the control group (Table 4).

Frequencies of cardiovascular risk factors (Table 5)

The frequencies of evaluated CV risk factors are summarized in Table 6. Two-thirds of the patients had anaemia and high HS-CRP levels. Uncontrolled BP and dyslipidaemia were prevalent in ∼45% of the patients.

Echocardiographic data of the patients (Table 6)

Cardiac function. When compared to the control subjects, EF, PWD and TDI E/A ratios were lower; IVRT, DT, PWD E/TDI E ratio and MPI were all found to be higher in patients on maintenance dialysis. The PWD E/TDI E ratio was positively correlated with MAP ($r = 0.229$, $P = 0.050$), CIMT ($r = 0.277$, $P = 0.014$) and LVMI ($r = 0.541$, $P = 0.000$), while negatively with residual urine volume ($r = -0.373$, $P = 0.005$) and haemoglobin ($r = -0.467$, $P = 0.000$). There were positive correlations between homocysteine and MPI ($r = 0.524$, $P = 0.018$).

A lower residual urine volume (β: −0.45, 95% CI: −0.869 to −0.034, $P = 0.034$) and increased CIMT (β: 5.90, 95% CI: 1.59–10.21, $P = 0.008$) were independent predictors of an increased PWD E/TDI E ratio reflecting diastolic dysfunction.

Table 7. Structural and functional cardiac parameters in patients with or without residual diuresis

	Oligo/anuric patients ($n = 28$)	Patients with residual diuresis ($n = 31$)	*P*-value
LVMI (g/m^2)	73 ± 32	52 ± 17	0.009
RWT (cm)	0.53 ± 0.13	0.45 ± 0.11	0.025
PWD E/A ratio	1.4 ± 0.3	1.6 ± 0.3	0.014
TDI E/A ratio	1.6 ± 0.5	2.0 ± 0.5	0.006
PWD E/TDI E ratio	9.6 ± 3.9	6.9 ± 2.3	0.004

Cardiac structure. LVMI and RWT were significantly higher in patients on maintenance dialysis compared to the controls (Table 6) and were negatively correlated with Kt/V urea ($r = -0.338$, $P = 0.022$ and $r = -0.305$, $P = 0.039$, respectively). LVMI was also found to be negatively correlated with haemoglobin (Hb) ($r = -557$, $P = 0.000$) and residual urine volume ($r = -0.306$, $P = 0.021$), while positively with HS-CRP ($r = 0.325$, $P = 0.0150$), ferritin ($r = 0.501$, $P = 0.000$) and CIMT ($r = 0.310$, $P = 0.019$). There were no correlations between LVMI and blood pressure, calcium–phosphorus product or PTH levels. Lower Hb levels were independent predictors of increased LVMI (β: −8.9, 95% CI: −12.5 to −5.3, $P = 0.001$). LVH was prevalent in 67.8% (54.2% concentric, 13.6% eccentric) of the patients. A total of 18.6% of the patients were normal and 13.6% had concentric remodelling. Patients with LVH (eccentric + concentric) had higher levels of HS-CRP [1.30, 0.03–8.61 versus 0.28, 0.04–1.60 mg/l, (median, range), $P = 0.001$] and CIMT (0.64 ± 0.10 versus 0.57 ± 0.15 mm, $P = 0.028$). There were no differences in cardiac and atherosclerotic/inflammatory parameters between concentric and eccentric hypertrophy groups. Similarly, blood pressure, Hb, albumin levels, residual urine or ultrafiltration volumes were not different in either group.

There were significant differences in structural and functional cardiac parameters in patients with and without residual diuresis, which indicates a positive impact of residual urine on LVH and diastolic dysfunction (Table 7). Additionally, patients with residual diuresis have higher Hb (10.8 ± 1.4 versus 8.9 ± 1.6 g/dl, $P = 0.000$) and HDL levels (53 ± 13 versus 42 ± 14 mg/dl, $P = 0.004$) compared with oligo/anuric patients. There were no differences in any routine laboratory parameters, atherosclerotic/inflammatory markers as well as cardiac structural and functional parameters in APD and CAPD patients, except relatively lower diastolic BP levels in APD patients.

Vascular structure. CIMT values were significantly higher in the patient group than in the control group

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(Table 4). CIMT levels were negatively correlated with Hb ($r = -0.428$, $P = 0.001$) and albumin levels ($r = -0.342$, $P = 0.009$) as well as Kt/V urea ($r = -0.382$, $P = 0.008$), while positively with MAP ($r = 0.272$, $P = 0.037$) and HS-CRP ($r = 0.283$, $P = 0.033$). Lower albumin (β: −0.72, 95% CI: −0.13 to −0.01, $P = 0.018$) and lower Kt/V urea (β: −0.48, 95% CI: −0.84 to −0.11, $P = 0.012$) were independent predictors of increased CIMT.

Discussion

We studied an extended panel of atherosclerotic/inflammatory CV risk markers including atherogenic lipids, homocysteine, HS-CRP and CIMT and found significantly elevated levels of all these markers in a large group of paediatric patients on maintenance PD. The patients had also disturbed structural and functional echocardiographic parameters that were found to be tightly related to those CV risk factors. In a recent review [1], Mitsnefes clearly signifies that there are two parallel processes involved in the development of CVD in CKD patients and our findings strongly correspond to his elucidation. The first process is cardiac remodelling leading to LVH as a response to mechanical or haemodynamic overload. The second process involves vascular injury. Exposure to CV risk factors results in vascular changes, including atherosclerotic and arteriosclerotic processes and vascular calcification [1]. They constitute strong independent predictors of cardiac morbidity and mortality in children with CKD [1–4].

The mortality rate in adults and children with CKD is markedly higher than that in the general population, and CVD is the leading cause of death in both children and adults treated with maintenance dialysis [23]. In contrast to adults, there is no clear evidence that high CV mortality rates among paediatric patients with ESRD are mainly attributed to atherosclerotic disease. However, atherosclerosis is nowadays recognized as a chronic inflammatory disease that begins in early childhood [8]. Furthermore, uraemia is a state of insulin resistance, which is a clear risk factor for arteriosclerosis [24]. The development of premature and accelerated arteriosclerosis in childhood is more likely in patients undergoing CPD due to the increased tendency towards dyslipidaemia [25], although this is not acknowledged in all studies [26]. Traditional CV risk factors such as hypertension, dyslipidaemia and non-traditional risk factors such as high CRP, hyperhomocysteinaemia and endothelial damage characterized by increased CIMT are common for both HD and PD patients [7,27].

Dyslipidaemia has been considered as one of the major causes of CVD in patients with CRF [7,15]. High-normal LDL-cholesterol and significantly higher apolipoprotein B and lipoprotein (a) levels indicated an atherogenic lipid profile in our patients. Hyperhomocysteinaemia and increased CIMT and HS-CRP were also detected in the patient group. Remarkably, higher MPI levels reflecting combined systolic and diastolic dysfunction in our patients were well correlated with homocysteine.

HS-CRP has also recently been suggested as a useful marker of vascular endothelial damage that leads to atherosclerosis [28]. Its levels can be used for estimating the development and severity of atherosclerosis. According to AHA recommendations [15], our patients had an average CV risk with their HS-CRP levels of 1.82 ± 0.42 mg/l. However, paediatric CKD patients are already in a high-risk category for premature CVD in the paediatric statement of AHA [29] and truly require the monitorization of HS-CRP. Recently, Pecoits-Filho *et al*. [30] showed a significantly higher level of inflammatory markers in adults with GFR <6.5 ml/min versus those with GFR between 6.5 and 16.5 ml/min. Goldstein *et al*. [31] showed that chronic inflammation is highly prevalent in paediatric patients on maintenance dialysis. It is also well established that chronic inflammation is associated with cardiac calcification and carotid arteriopathy in young adults with CKD [10]. In our study, high HS-CRP was prevalent in 66% of the patients and was significantly associated with both higher LVMI and CIMT. It indicates the effect of inflammation on cardiac and vascular remodelling. Statins may exhibit dual action on the atherogenesis by a reduction of lipids as well as CRP and IL-6 [32]. Ikejiri showed a marked decrease in HS-CRP levels with atorvastatin in HD patients suggesting statins' direct suppressive effect on microinflammation and atherosclerosis [33]. We had 14 patients on statins and they did not show any significant difference in HS-CRP levels and in functional cardiac parameters. Another option might be sevelamer for suppressing inflammation and decreasing lipids. A recent study demonstrated well that sevelamer can be a promising therapy for CV risk reduction rather than statins by reducing LDL-cholesterol and CRP levels in adult HD patients [34]. Furthermore, sevelamer was shown to suppress the progression of aortic calcification in HD patients [35].

In recent years, CIMT has been validated for the assessment of cardiovascular pathology in children with CKD, which occurs early in the course of disease and is most marked in dialysed patients [10,36,37]. Kt/V urea and serum albumin were independent predictors of CIMT in our study. Albumin is considered a positive CV risk factor like HDL-cholesterol. Low albumin levels, one of the main determinants of malnutrition–inflammation–atherosclerosis (MIA) syndrome, is a strong predictor of mortality in patients on maintenance dialysis [38]. A recent longitudinal study showed that higher CIMT and CRP and lower serum albumin levels predict long-term mortality in adult ESRD patients [39]. Forty-four percent of our patients had suboptimal levels of albumin. Therefore, measures targeting higher albumin levels might alleviate arteriopathy in our patients. Indeed, abolition of the uraemic state by renal transplantation leads to stabilization or partial regression of CKD-associated arteriopathy and LVH [40]. Significant associations between the cardiac structure (LVMI) and the vascular structure (CIMT) in our study suggest a universal adaptation of the CV system in PD patients, as previously demonstrated by Mitsnefes *et al*. [36]. Furthermore, that our patients with LVH had higher levels of HS-CRP and CIMT when compared to those without LVH confirms the previously indicated link between CIMT, HS-CRP and LVH in both dialysed and CKD patients [41,42].

Interrelationships between cardiac and vascular hypertrophy in adults with primary hypertension and with ESRD

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suggested that pressure and volume overload might be involved in the development of both vascular and myocardial abnormalities [43,44]. In our study, unlike in adults, BP was not a predictor of LVMI, as was in Mitsnefes's paediatric study [36] possibly due to the multicentre nature of our study and less reliable results of casual BP recordings. However, diastolic dysfunction and vascular remodelling were associated with MAP levels. Additionally, MAP was demonstrated as a risk factor for CIMT and HS-CRP elevation.

The main determinant of LVH in our study was serum Hb concentrations. The prevalence of LVH was 68% in the present study, and it has been varied between 69 and 79% in different Turkish studies [16,20,41]. This is somewhat higher than in European and American studies. This seems to be mostly related to higher Hb levels in those patients compared to Turkish patients (>11 g/dl versus <10 g/dl) [45–47]. In addition to an abnormal cardiac structure (increased LVMI), diastolic dysfunction (higher PWD E/TDI E ratio) and abnormal vascular structure (increased cIMT) were significantly related to anaemia.

The conventional PWD technique is limited to measurement of transmitral flow velocities and IVRT [48], and also dependent on heart rate, sampling site and loading conditions. Pulsed-TDI, which evaluates regional myocardial function by recording systolic/diastolic velocities within the myocardium, is relatively independent of loading conditions and thus better reflects diastolic function [49]. However, even when using TDI, predialysis overhydration in haemodialysis patients leads to a high preload, which may mask impairment of early diastolic filling [50,51]. A significant influence of preload on echocardiography indexes is demonstrated also in normal subjects [52]. To our knowledge, no data are available in PD patients. It is important to note that volume status was not assessed in our patients. Theoretically, PD is a dialytic therapy that provides relatively sustained volume status without big fluctuations compared to HD. We performed echocardiographic studies after a standard PD schedule. Nevertheless, one cannot exclude that PD-induced preload changes may have affected results in this study. In our study, an increased PWD E/TDI E ratio as a relatively reliable measure of impaired diastolic function was detected in the patient group. A lower residual urine volume was an independent risk factor for diastolic dysfunction in our patient group. Additionally, there were significantly higher levels of LVMI and diastolic dysfunction parameters in oligo/anuric patients compared to the patients with some residual diuresis. Recently, Wang *et al*. clearly demonstrated that residual renal function and CRP levels were independent predictors of LVMI; all three variables are the main determinants of CV and all cause mortality of the patients [53]. Moreover, a fast decline in RRF has been suggested as a more powerful prognostic factor than baseline RRF associated with all-cause mortality and technique failure in adults on long-term PD [54]. Therefore, preserving RRF is of vital importance by preventing overdiuresis, peritonitis and hypotensive episodes as well as limiting the use of nephrotoxic medications. Since the current literature supports PD as having a more beneficial effect on RRF [55], the preserving peritoneal membrane is also the main issue.

Adequate dialyses (higher Kt/V urea) were shown to be related to lower risk for cardiac and vascular remodelling characterized by lower LVMI and CIMT in this study. It was previously shown that adequate dialysis resulted in decreasing LV diameters and septal thicknesses in paediatric CPD patients [18]. In adult patients on maintenance PD, higher time-averaged CRP levels were associated with both LVH and all-cause mortality. Furthermore, lower Kt/V urea was independently associated with the time course of serum CRP sustained high or increased from normal to high [56]. Therefore, adequate dialysis may contribute to reducing the incidence of inflammation and subsequent CVD in PD patients. Therefore, pursuing higher target clearances should be one of our main tasks to achieve better CV health.

In conclusion, this study has clearly shown that LVH and diastolic dysfunction are highly prevalent and strongly related to residual diuresis, dialysis adequacy and early arteriosclerotic markers as well as traditional CV risk factors in children on PD. For decreasing CVD, optimal control of BP and volume status, optimal correction of anaemia, dyslipidaemia and hypoalbuminaemia, achieving recommended targets for Kt/V urea, better preservation of residual diuresis and managing inflammation are of particular significance. Potential therapeutic strategies such as statins, folate, sevelamer, etc. for managing inflammation could be investigated in further longitudinal studies.

Conflict of interest statement. None declared.

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