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Changes in left ventricular mass in children and adolescents during chronic dialysis

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Abstract Left ventricular hypertrophy (LVH) is an independent risk factor for cardiac mortality in adults with end-stage renal disease (ESRD). It is prevalent in pediatric patients on chronic dialysis. The objectives of this study were to evaluate left ventricular mass (LVM) in children and adolescents at the initiation of dialysis and to assess its changes during chronic dialysis therapy. In this longitudinal analysis, 29 patients aged 4–18 years had an echocardiographic evaluation within 90 days of starting dialysis therapy and a follow-up study at least 6 months later. LVH was defined as LVM index ($g/m^{2.7}$) >95th percentile for normal children and adolescents. On the initial echocardiogram 20 of 29 (69%) patients had LVH and 24 patients (83%) had abnormal LV geometry (38% eccentric LVH, 31% concentric LVH, and 14% concentric remodelling). Patients with LVH were more likely to be on antihypertensive medications (16/20) than patients without LVH (3/9) (P=0.005). Repeat echocardiogram, performed after 10±3 months on chronic dialysis, showed no significant difference in the mean LVM index (49.6±17.5 $g/m^{2.7}$ and 49.7±16.1 $g/m^{2.7}$, respectively) or in the prevalence of LVH or LV geometric pattern. However, 14 of 29 patients had a progressive increase in LVM index and 15 patients had regression. Multiple regression analysis showed that baseline LVM index (P=0.005) and interval change in indexed systolic blood pressure (P=0.027) were independent predictors for LVM index changes. In summary, LVH and abnormal LV geometry are already prevalent in children and adolescents with renal failure at the time of initiation of dialysis therapy, indicating that LVH develops during the pre-ESRD course. Early intervention to control blood pressure may be an important factor to improve and prevent progression of LVH in pediatric patients with ESRD.

Keywords Pediatric dialysis · Cardiac disease · Left ventricular hypertrophy · Hypertension

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Introduction

Left ventricular hypertrophy (LVH) is the most-common cardiac abnormality in adults with end-stage renal disease (ESRD) and has been identified as one of the strongest independent predictors of increased cardiovascular mortality in these patients [1, 2, 3, 4]. As in adults, young patients with ESRD have been previously described to have LV abnormalities [5, 6, 7, 8, 9, 10]. The prevalence of LVH in children and adolescents on dialysis is similar to adults. In a recent cross-sectional analysis, we showed that 75% of young patients on chronic dialysis had LVH, 80% had abnormal LV geometry, and 41% had severe LVH [11].

In adult ESRD patients, LVH is most commonly identified at the time dialysis is initiated and may progress during long-term dialysis [12, 13, 14, 15, 16, 17]. However, in pediatric patients it is not currently known when in the course of ESRD and dialysis LVH develops and whether it progresses or regresses during long-term dialysis. The purpose of this study was to evaluate LV mass (LVM) and LV geometry in children and adolescents soon after the initiation of chronic dialysis and assess changes in cardiac size during chronic dialysis therapy.

Table 1 Patient characteristics (*M* male, *F* female, *W* white, *B* black, *ESRD* end-stage renal disease, *HD* hemodialysis, *PD* peritoneal dialysis, *NS* not significant)

Variable	Patient subset (*n*=29)	Excluded patients (*n*=14)	*P* value
Age, years[a] (range)	13.8±3.7 (4–18)	14.5±2.8 (7–17)	NS
Sex (M/F)	13/16	6/8	NS
Race (W/B)	17/12	10/4	NS
Cause of ESRD (glomerular, cystic/others)	16/13	8/6	NS
Type of dialysis (HD/PD)	13/16	5/9	NS
Hypertension	23/29	10/14	NS
Anemia	15/29	6/14	NS

[a] Data presented as mean±SD

Materials and methods

Subjects

Clinical, laboratory, and echocardiographic data were obtained retrospectively from the medical records of 43 chronic dialysis patients, 4–18 years old, who started dialysis at The Children's Hospital Medical Center, Cincinnati, between January 1994 and December 1999. The inclusion criteria were a baseline echocardiographic evaluation within 90 days of starting dialysis and a follow-up echocardiogram at least 6 months later. Twenty-nine patients were included for analysis. Among the 14 patients that were excluded, 8 had their first echocardiogram after 90 days on dialysis, 3 had a renal transplant prior to 6 months follow-up, and 3 were on dialysis less than 6 months. The medical records were reviewed for age, sex, race, type of dialysis modality, cause of ESRD, and duration of renal failure prior to starting dialysis. Clinical and laboratory data were collected on the day of the echocardiographic evaluation (before dialysis in hemodialysis patients) including height, weight, systolic (SBP) and diastolic (DBP) blood pressure, quantitative urea kinetics (Kt/V), serum creatinine, blood urea nitrogen, calcium, phosphorus, albumin, hemoglobin, and intact parathyroid hormone (iPTH).

Blood pressure

The mean of monthly SBP and DBP measurements for up to 6 months preceding the echocardiogram was calculated. SBP and DBP were also indexed to the age-, sex-, and height-specific 95th percentile for each subject (measured SBP or DBP was divided by the age-, sex-, and height-specific 95th percentile SBP or DBP) [18]. This standardizes blood pressure for differences in age and size. Hypertension was defined as SBP, DBP, or both greater than the 95th percentile for sex, age, and height, or indexed SBP and DBP >1.0. Hypertension was also assessed by the use of blood pressure medications.

Echocardiography

Each patient had echocardiography as a part of routine evaluation after starting dialysis. Echocardiograms were performed using standard techniques. LVM was measured by two-dimensional directed M-mode echocardiography according to the American Society of Echocardiography criteria [19]. LVM index ($g/m^{2.7}$) was used to evaluate LVH accounting for body size, as described elsewhere [20]. Significant change in LVM index was defined as relative change of greater than 20% from the baseline value. LVH was defined as LVM index greater than the 95th percentile for normal children and adolescents [21]. Children younger than 4 years were not included for analysis since the norms for LVM index for this age are not well defined. Relative wall thickness (RWT) was measured to assess the LV geometric pattern [22]. Patients with LVH and elevated RWT (>0.41) had concentric LVH, those with LVH and normal RWT (<0.41) had eccentric LVH. Concentric remodelling was defined as elevated RWT, but with normal LVM index.

Statistical analysis

The *t*-test or *t*-test for paired samples was used to compare means±SD for continuous variables and the chi-squared or exact Fisher tests were used to compare categorical variables. Stepwise multiple regression analysis was performed to assess potential independent predictors for LVM index at the time of initiation of dialysis, as well as for LVM index changes. Potential predictor variables included age, sex, type of dialysis (hemodialysis vs. peritoneal dialysis), cause of ESRD (glomerular and cystic disease vs. others), duration of chronic renal failure (<6 months vs. >6 months) prior to initiation of dialysis, Kt/V, use of antihypertensive medications, and baseline or changes in clinical or laboratory variables (indexed SBP, indexed DBP, hemoglobin, creatinine, albumin, and iPTH). The associations between variables were assessed by Pearson correlation analysis. A P value ≤0.05 was considered statistically significant.

Results

There was no significant difference between the patient subset and children who were excluded from the study (Table 1). The causes of ESRD included glomerular disease (13 patients), renal dysplasias/obstructive uropathies (7 patients), cystic diseases (3 patients), metabolic disorders (2 patients), cortical necrosis and nephrotoxicity (3 patients), and congenital nephrotic syndrome (1 patient). No patients had the dialysis modality changed during the follow-up period. At the time of initiation of dialysis, 23 (79%) patients had systolic hypertension and 15 (52%) diastolic hypertension. Nineteen (66%) patients were treated with antihypertensive medications: 13 patients were taking a single medication, 5 were taking two, and 1 was taking three medications. Antihypertensive medications prescribed included calcium channel blockers (13 patients), β-blockers (7 patients), and angiotensin converting enzyme inhibitors (ACEI) (4 patients).

The initial baseline (mean duration on dialysis 1.8±1.2 months) and follow-up (10.3±2.9 months) clinical, laboratory, and echocardiographic parameters are compared in Table 2. Twenty (69%) patients had LVH and 24 (84%) had abnormal LV geometry at baseline. The clinical and laboratory values from 20 patients with LVH were compared with those from 9 patients with a normal LVM index at their initial evaluation. There was no significant difference in any of the clinical or laboratory parameters, as well as in the cause of kidney failure (glomerular and cystic disease versus others, P=0.59) or duration of renal insufficiency (<6 months versus >6

Table 2 Changes in clinical, laboratory, and echocardiographic parameters from baseline to the first follow-up echocardiogram (29 patients) (*BMI* body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *iPTH* intact parathyroid hormone, *BUN* blood urea nitrogen, *LVM* left ventricular mass, *LVH* left ventricular hypertrophy)[a]

Variable	Baseline	Follow-up	*P* value
BMI	19.8±5.4	20.1±5.3	NS
SBP (mmHg)	134.7±23.58	133.7±20.3	NS
DBP (mmHg)	79.0±15.5	82.7±14.5	NS
Indexed SBP	1.12±0.12	1.10±0.16	NS
Indexed DBP	1.03±0.16	1.04±0.18	NS
BUN (mg/dl)	63.2±24.1	52.1±13.1	0.01
Serum creatinine (mg/dl)	9.9±3.6	11.6±3.5	0.001
Hemoglobin (g/dl)	9.4±1.6	10.5±2.1	0.004
iPTH (pg/dl)	564.4±326.2	352.6±405.0	0.07
Serum albumin (g/dl)	3.29±0.50	3.59±0.47	0.02
LVM index (g/m$^{2.7}$)	49.6±17.5	49.7±16.1	NS
Prevalence of LVH (%)	69	70	NS
LV geometry (%)			
Eccentric	38	38	NS
Concentric	31	32	NS
Concentric remodelling	14	13	NS
Normal	17	17	NS

[a] Data presented as mean±SD

Table 3 Comparison of progression and regression groups at baseline[a]

Variable	Regression (*n*=15)	Progression (*n*=14)	*P* value
Age (years)	13.8±4.8	12.7±4.1	0.20
Weight (kg)	52.9±23.7	40.9±20.7	0.06
BMI	20.8±6.1	18.6±4.7	0.13
SBP (mmHg)	140.1±26.0	127.6±19.5	0.06
DBP (mmHg)	81.1±17.0	76.7±14.0	0.52
Hemoglobin (g/dl)	9.4±1.6	9.5±1.6	0.93
Creatinine (mg/dl)	10.2±3.4	9.5±3.9	0.51
BUN (mg/dl)	68.0±27.1	58.0±20.1	0.48
iPTH (pg/ml)	501.4±367.8	645.0±252.5	0.14
Duration on dialysis (years)	0.14±0.09	0.18±0.13	0.44
LVM index (g/m$^{2.7}$)	57.3±19.6	41.4±10.1	0.04

[a] Data presented as mean±SD

Table 4 Changes in clinical and laboratory parameters in patients with progression or regression of LVM index[a]

Variable	Regression (*n*=15) Δ 2–1[b]	Progression (*n*=14) Δ 2–1
Weight (kg)	2.5±9.4	2.3±5.8
	P=0.34	*P*=0.16
BMI	0.46±3.5	0.6±2.4
	P=0.62	*P*=0.36
SBP (mmHg)	–10.1±19.7	10.0±17.1
	P=0.07	*P*=0.05
DBP (mmHg)	2.0±13.6	5.5±15.3
	P=0.57	*P*=0.20
Hemoglobin (g/dl)	1.2±1.8	1.0±2.1
	P=0.02	*P*=0.09
Creatinine (mg/dl)	1.6±2.2	1.8±2.8
	P=0.02	*P*=0.03
BUN (mg/dl)	–14.4±26.2	–7.6±18.3
	P=0.05	*P*=0.14
iPTH (pg/ml)	–282.3±356.8	–177.8±466.1
	P=0.11	*P*=0.44
Albumin	0.28±0.63	0.32±0.56
	p=0.16	p=0.09
LVM index (g/m$^{2.7}$)	–14.4±10.1	15.7±8.9
	P=0.0001	*P*=0.0001

[a] Data presented as mean±SD
[b] Δ 2–1, difference between follow-up and initial evaluation

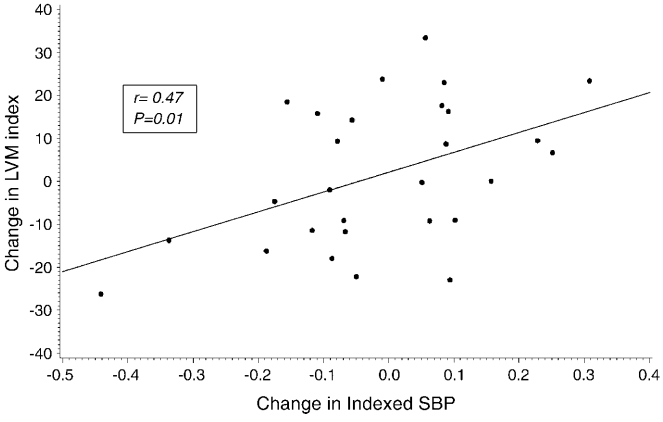

Fig. 1 The change from baseline to follow-up in left ventricular mass (*LVM*) index (g/m$^{2.7}$) is plotted against the change in indexed systolic blood pressure (*SBP*) for each patient

months, *P*= 0.54) between the two groups. However, significantly more patients with LVH (16/20) were treated with antihypertensive medication than patients without LVH (3/9) (*P*=0.005).

At the time of the second echocardiogram, the prevalence of systolic and diastolic hypertension remained high (69% and 55%, respectively). The number of patients with anemia decreased significantly (37.5%). There was no significant difference in the mean LVM index or in the prevalence of LVH or LV geometric patterns on the repeat examination compared with baseline. In addition, there was no difference in the mean LVM index between hemodialysis and peritoneal dialysis patients on the follow-up evaluation (*P*=0.76).

Despite no significant difference in the mean values of LVM index between the initial and follow-up echocardiograms for the group as a whole (*P*=0.9), 14 (48%) patients had an increase in LVM index (progression group) and 15 (52%) had a decrease in LVM index (regression group). In 6 of the 14 patients (43%) who had an increase in LVM index and in 5 of the 15 patients (33%) who had a decrease in LVM index, the change was greater than 20%. As shown in Table 3, the initial or baseline clinical and laboratory parameters, including blood pressure and hemoglobin level, were similar between the progression and regression groups. However, patients who had regression in LVM index had a higher LVM index (57.3± 19.6 g/m$^{2.7}$ vs. 41.4±10.1 g/m$^{2.7}$, *P*=0.04) at the onset of dialysis. The changes in clinical and laboratory characteristics between the baseline and follow-up echocardiographic studies for regression and progression groups are shown in Table 4. Correlation analysis was performed to

Table 5 Changes in LV geometry in patients with progression or regression of LVM index

Variable	Regression (*n*=15)		Progression (*n*=14)	
	Baseline	Follow-up	Baseline	Follow-up
Eccentric, *n* (%)	6 (40)	5 (34)	5 (36)	6 (43)
Concentric, *n* (%)	6 (40)	2 (13)	3 (21)	7 (50)
Concentric remodelling, *n* (%)	0	3 (20)	4 (29)	1 (7)
Normal, *n* (%)	3 (20)	5 (33)	2 (14)	0

evaluate factors associated with the change in LVM index between the initial and follow-up echocardiograms. The change in LVM index correlated significantly with interval changes in indexed SBP (Fig. 1). Stepwise multiple regression analysis showed that baseline LVM index (β=–0.49, *P*=0.005) and interval change in indexed SBP (β=42.7, *P*=0.026) were significant independent predictors for change in LVM index. The direction of the associations in this regression model indicates that those patients who had a lower baseline LVM index and an increase of SBP from the initial to follow-up evaluation are most likely to have an increase in LVM index.

The changes in LV geometric patterns from the baseline to the follow-up in progression and regression groups are shown in Table 5. The patients who had regression of LVH did so mostly by a decrease in concentric LVH (from 40% to 13%), whereas those patients with an increase of LVH mostly progressed to concentric LVH on follow-up (from 21% to 50%).

Discussion

This study is the first to report longitudinal changes in LVM in pediatric patients with ESRD. The important observation in this study is that LVH and abnormal LV geometry are prevalent in children at the time of initiation of dialysis. This observation is similar to that of other investigations in adult patients [12] and supports the concept that LV abnormalities in patients with ESRD occur under uremic conditions independent of age. Although at baseline there was no significant difference in blood pressure in patients with and without LVH, the patients with LVH required significantly more antihypertensive medications than those without LVH. This suggests that in children with LVH hypertension was more difficult to control at time of entry into dialysis. A longer duration of chronic renal failure prior to initiation of dialysis or the presence of hypertensive renal diseases (glomerular or cystic) might be expected to be associated with LVH. However, our analysis failed to reveal these relationships. This may be due to limited power because of the small sample size. An additional limitation is the absence of measured residual renal function at the time of initiation of dialysis. Patients with remaining residual renal function might be expected to have less LVH. Future prospective studies will be necessary to examine this association.

The impact of long-term dialysis on LVM remains unclear. Previous investigators have found regression [23, 24, 25, 26], progression [13, 14, 15, 16, 17] and no change [27, 28] in LVH during dialysis in adults. Anemia and hypertension have consistently been found to be the important predictors of change in LVM. Foley et al. [14] reported a prospective cohort study of 29 ESRD patients who had four serial echocardiograms at yearly intervals. LVH continued to progress after the institution of dialysis. Risk factors for progression of LVH were hemodialysis, as opposed to peritoneal dialysis, and the presence of anemia. No such association with type and adequacy of dialysis or anemia was present in our study. In fact, improvement in hemoglobin concentration was observed in both the regression and progression groups. Despite relatively short follow-up, 11 of 29 patients (38%) had more than a 20% change in LVM index from baseline. These results are in agreement with adult studies showing that significant changes in LVM and LV geometry might occur within the 1st year after initiation of dialysis. For example, Foley et al. [14] showed that the majority of change in LVM index occurred in the 1st year of follow-up after starting dialysis. Lennen et al. [23] demonstrated that control of blood pressure resulted in significant regression of LVM within a few months of initiation of chronic ambulatory peritoneal dialysis in adults. These authors also showed that the regression of LVH was due to decrease in both eccentric and concentric LVH. The proposed reason for these changes was the marked swings in extracellular fluid volume associated with initiation of dialysis.

Our results, although limited by small patient population and short duration of follow-up, show that the factors most likely to influence the increase of LVM are lower baseline LVM index and increase in SBP over time. These data are concordant with adult studies. For example, Levin et al. [29] showed that lower LVM index predicted an increase in LVM in patients with chronic renal failure. They speculated that patients with lower baseline LVM index might have a greater potential for LVM growth in the presence of uremia, hypertension, and decreased hemoglobin. One of the elements that could contribute to these relationships might be statistical regression toward the mean. However, after controlling for baseline LVM index, change in SBP was still an independent predictor for LVM change in our study. The importance of blood pressure control is also supported by analysis of specific geometric patterns observed in our patients. Concentric LV remodelling and hypertrophy may be related to pressure overload as occurs with hypertension, whereas eccentric LV hypertrophy may be related to volume overload, as frequently seen in patients on dialysis or with anemia [30]. In our study, both eccen-

tric and concentric LVH were already prevalent at the time of initiation of dialysis. The high prevalence of these abnormal LV geometric patterns is likely to reflect the clinical status of the studied population, where 79% had hypertension and 52% were anemic with a hemoglobin level less than 10 g/dl at the baseline evaluation. The patients who had regression of LVH did so mostly by a decrease in concentric LVH, whereas those patients with an increase of LVH mostly progressed to concentric LVH on follow-up. This observation suggests that change in pressure rather than volume is the driving force for change in LVM over time in these patients. The data also indicate that despite the regression of LVH, normalization of LV geometry is unlikely, since most of the patients with concentric LVH regressed to the concentric remodelling geometric pattern. Only 1 patient, who had eccentric LVH and 1 with concentric LVH at baseline, reverted to normal geometry. Some studies [31, 32] propose that the use of ACEI might be associated with LV remodelling and greater regression of LVH compared with the use of other antihypertensives. In this study we could not evaluate the effect of ACEI on changes of LVH since only 4 children were taking ACEI.

The results of this study demonstrate that LVH is highly prevalent in children and adolescents at the initiation of chronic dialysis therapy. This observation indicates that LVH develops during the course of chronic renal failure, prior to the need for dialysis. Our results also demonstrate that LV abnormalities persist during chronic dialysis, but that LVM may change significantly over time for a specific patient. Serial echocardiography starting before initiation of dialysis, and the recognition and aggressive treatment of potential risk factors, such as systolic hypertension, may be important initial steps in improving or preventing LVH in children and adolescents with ESRD, thereby decreasing cardiovascular risk.

References

1. The USRDS 1998 Annual Report (1998) Causes of death. Am J Kidney Dis 32 [Suppl 1]:S81–S88
2. Foley RN, Parfrey PS, Sarnak MJ (1998) Clinical epidemiology of cardiovascular disease in chronic renal disease. Am J Kidney Dis 32 [Suppl 3]:S112–S119
3. Silberberg JS, Barre PE, Prichard SS, Sniderman AD (1989) Impact of LVH on survival in end-stage renal disease. Kidney Int 36:286–290
4. Foley RN, Parfrey PS, Harnett JD, Kent GM, Murray DC, Barre PE (1995) The prognostic importance of left ventricular geometry in uremic cardiomyopathy. J Am Soc Nephrol 5:2024–2031
5. The USRDS 1998 Annual Report(1998) Pediatric end-stage renal disease. Am J Kidney Dis 32 [Suppl 1]:S98–S108
6. Johnstone LM, Jones CL, Grigg LE, Wilkinson JL, Walker RG, Powell HR (1996) Left ventricular abnormalities in children, adolescents and young adults with renal disease. Kidney Int 50:998–1006
7. Loirat C, Ehrich JHH, Geerlings W, Jones EHP, Landais P, Mallick NP, Margreiter R, Raine AEG, Salmela K, Selwood NH, Tufveson G, Valderrabano F (1994) Report on management of renal failure in children in Europe, XXIII, 1992. Nephrol Dial Transplant [Suppl 1]:26–40
8. Morris KP, Skinner JR, Wren C, Hunter S, Coulthard MG (1993) Cardiac abnormalities in end stage renal failure and anaemia. Arch Dis Child 68:637–643
9. O'Regan S, Matina D, Ducharme G, Davignon A (1983) Echocardiographic assessment of cardiac function in children with chronic renal failure. Kidney Int [Suppl 15]:77–82
10. Drukker A, Urbach J, Glaser J (1981) Hypertrophic cardiomyopathy in children with end-stage renal disease and hypertension. Proc Eur Transplant Assoc 18:542–547
11. Mitsnefes MM, Daniels SR, Schwartz SM, Khoury P, Meyer RA, Strife CF(2000) Severe left ventricular hypertrophy in pediatric dialysis: prevalence and predictors. Pediatr Nephrol 14:898–902
12. Foley RN, Parfrey PS, Harnett JD, Kent GM, Martin CJ, Murray DC, Barre PE (1995) Clinical and echocardiographic disease in patients starting end-stage renal disease therapy. Kidney Int 47:186–192
13. Huting J, Alpert MA (1992) Progression of left ventricular hypertrophy in end-stage renal disease treated by continuous ambulatory peritoneal dialysis depends on hypertension and hypercirculation. Clin Cardiol 15:190–196
14. Foley RN, Parfrey PS, Kent GM, Harnett JD, Murray DC, Barre PE (1998) Long-term evolution of cardiomyopathy in dialysis patients. Kidney Int 54:1720–1725
15. Huting J, Kramer W, Schutterle G, Wizemann V (1988) Analysis of left-ventricular changes associated with chronic hemodialysis: a noninvasive follow-up study. Nephron 49:284–290
16. Parfrey PS, Harnett JD, Griffiths SM, Taylor R, Hand J, King A, Barre PE (1990) The clinical course of left ventricular hypertrophy in dialysis patients. Nephron 55:114–120
17. Eisenberg M, Prichard S, Barre P, Patton R, Hutchinson T, Sniderman A (1987) Left ventricular hypertrophy in end-stage renal disease on peritoneal dialysis. Am J Cardiol 60:418–419
18. Kimball TR, Daniels SR, Loggie JMH, Khoury P, Meyer RA (1993) Relation of left ventricular mass, preload, afterload and contractility in pediatric patients with essential hypertension. J Am Coll Cardiol 21:997–1001
19. Devereux RB, Reichec N (1977) Echocardiographic determination of left ventricular mass in man: anatomic validation of the method. Circulation 55:613–618
20. De Simone G, Daniels SR, Devereux RB, Meyer RA, Roman MJ, Divitis O de, Alderman MH (1992) Left ventricular mass and body size in normotensive children and adults: assessment of allometric relations and impact of overweight. J Am Coll Cardiol 20:1251–1260
21. De Simone G, Devereux RB, Daniels SR, Koren MJ, Meyer RA, Laragh JH (1995) Effect of growth on variability of left ventricular mass: assessment of allometric signals in adults and children and their capacity to predict cardiovascular risk. J Am Coll Cardiol 25:1056–1062
22. Ganau A, Devereux RB, Roman MJ, Simone G de, Pickering TG, Saba PS, Vargiu P, Simongini I, Laragh JH (1992) Patterns of left ventricular hypertrophy and geometric remodeling in essential hypertension. J Am Coll Cardiol 19:1550–1558
23. Lennen FH, Smith DL, Khanna R, Oreopoulos DG (1985) Changes in left ventricular hypertrophy and function in hypertensive patients started on continuous ambulatory peritoneal dialysis. Am Heart J 110:102–106
24. Cannella G, Paoletti E, Delfino R, Peloso GC, Molinari S, Traverso GB (1993) Regression of left ventricular hypertrophy in hypertensive dialyzed uremic patients on long-term antihypertensive therapy. Kidney Int 44:881–886
25. Deligiannis A, Paschalidou E, Sakeellariou G, Vargemezis V, Geleris P, Kontopoulous (1984) Changes in left ventricular anatomy during hemodialysis, continuous ambulatory peritoneal dialysis and after renal transplantation. Proc Eur Dial Transplant Assoc 21:185–189
26. Silberberg JS, Racine N, Barre PE, Sniderman A (1990) Regression of left ventricular hypertrophy in dialysis patients following correction of anemia with recombinant human erythropoietin. Can J Cardiol 6:1–4

27. Morris KP, Skinner JR, Hunter S, Coulthard MG (1994) Cardiovascular abnormalities in end stage renal failure: the effect of anaemia or uremia? Arch Dis Child 71:119–122
28. London GM, Fabiani F, Marchais SJ, De Vernejoul MC, Guerin AP, Safar ME, Metivier F, Llach F (1987) Uremic cardiomyopathy: an inadequate left ventricular hypertrophy. Kidney Int 31:973–980
29. Levin A, Thompson CR, Ethier J, Carliste EJ, Tobe S, Mendelssohn D, Burgess E, Jindal K, Barrett B, Singer J, Djurdiev O (1999) Left ventricular mass index increase in early renal disease: impact of decline in hemoglobin. Am J Kidney Dis 34:125–134
30. London G, Parfrey PS (1997) Cardiac disease in chronic uremia: pathogenesis. Adv Renal Replace Ther 4:194–211
31. Cannella G, Paoletti E, Delfino R, Peloso G, Rolla D, Molinari S (1997) Prolonged therapy with ACE inhibitors induces a regression of left ventricular hypertrophy of dialyzed uremic patients independently from hypotensive effects. Am J Kidney Dis 30:653–664
32. Dydyk AI, Bagry AE, Lebed IA, Yarovaya NF, Shukina EV, Taradin GG (1997) ACE inhibitors captopril and enalapril induce regression of left ventricular hypertrophy in hypertensive patients with chronic renal failure. Nephrol Dial Transplant 12:945–951

LITERATURE ABSTRACTS

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Angiotensin I-converting enzyme gene insertion/deletion and angiotensinogen M235T polymorphisms: risk of chronic renal failure. End-Stage Renal Disease Study Group

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Background Chronic renal failure (CRF) is a complex phenotype that results from an underlying kidney disease and superimposing environmental and genetic factors. The aim of our study was to evaluate the role of polymorphisms in the genes encoding for components of the renin-angiotensin system (RAS) in the development and/or progression of CRF.
Methods Two hundred forty-seven family trios (patients with CRF and both parents; 120 with primary chronic glomerulonephritis, 80 with interstitial nephritis, and 47 with type 1 diabetes with nephropathy) were examined, and transmission/disequilibrium test (TDT) was used to evaluate allele transmission from heterozygous parents to affected offspring.
Results The D allele of the angiotensin I-converting enzyme (ACE) gene insertion/deletion polymorphism was transmitted significantly more frequently than expected for no association among all examined trios and in the subgroup of patients with interstitial nephritis. The angiotensinogen 235T allele was transmitted significantly more frequently to patients with CRF than expected for no association, but the effect was seen only in patients with interstitial nephritis. The presence of the DD or ID genotype was associated with a faster rate of decline of renal function, which was not observed for the angiotensinogen M235T polymorphism. For chymase gene and angiotensin II receptor type 1 gene, allele transmission did not deviate significantly from a random proportion of 50:50%.
Conclusions The results of this study suggest that ACE gene insertion/deletion and angiotensinogen M235T polymorphisms contribute to the increased risk for the development of CRF, but the magnitude of the effect within subsets of patients with specific etiologies of CRF must be evaluated further.

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Logarithmic extrapolation of a 15-minute postdialysis BUN to predict equilibrated BUN and calculate double-pool Kt/V in the pediatric hemodialysis population

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Blood urea nitrogen (BUN) concentration rebounds logarithmically for 1 hour after a hemodialysis treatment. We have previously devised and evaluated an equilibrated Kt/V (eqKt/V) estimation method using logarithmic extrapolation of the BUN increase from 30 seconds to 15 minutes postdialysis in six pediatric hemodialysis patients. The current study evaluates logarithmic extrapolation in 15 additional pediatric patients. Mean measured equilibrated BUN (eqBUN) and estimated BUN at equilibrium (estBUN) using logarithmic extrapolation were 23.1±9.2 and 23.0±9.4 mg/dL, respectively. The mean absolute difference between estBUN and eqBUN was 0.7±0. 4 mg/dL (range, 0.1 to 1.55 mg/dL). All treatments had an absolute difference less than the SD of the laboratory measurement itself. The mean absolute percentage of difference between eqKt/V using eqBUN and estimated double-pool equilibrated Kt/V (estKt/V) using estBUN from logarithmic extrapolation was 3.4%±2.3% and did not vary as a function of patient size, urea generation rate, dialyzer urea clearance, Kd/V, or ultrafiltration fraction. Mean absolute percentages of difference between eqKt/V and Kt/V estimated by the Tattersall, Daugirdas, or Maduell formulas were 4.5%±3.9%, 4.4%±3.7%, and 6.7%±8.3%, respectively. Total percentages of error (absolute mean percentage of error+2 SD) between eqKt/V and estKt/V by logarithmic extrapolation or the Tattersall, Daugirdas, or Maduell formulas were 8.0%, 12.3%, 11.8%, and 22.3%, respectively. The greater accuracy of logarithmic extrapolation compared with other methods of double-pool Kt/V estimation held true for patients weighing less than 35 kg. We have validated the use of an easy and accurate method requiring only an additional 15-minute posttreatment BUN level to estimate double-pool Kt/V in children.