J Korean Med Sci 1998; 13: 488-94
ISSN 1011-8934

Prevalence and Patterns of Left Ventricular Hypertrophy in Patients with Predialysis Chronic Renal Failure

Left ventricular hypertrophy (LVH) is an independent risk factor for cardiac death. This study evaluates the prevalence and patterns of LVH in patients with predialysis chronic renal failure (CRF) and analyses the relationship between LVH and various predisposing factors. Sixty-two CRF patients were recruited from the renal clinic with serum creatinine over 2 mg/dl. Using echocardiography, we calculated the left ventricular mass index (LVMI) and relative wall thickness (RWT), and classified the patients into four groups (Group 1: normal, Group 2: concentric remodelling, Group 3: concentric hypertrophy, Group 4: eccentric hypertrophy). Prevalence and patterns of LVH in patients with CRF were as follows; 6.5% in Groups 1 and 2, 56.5% in Group 3 and 30.5% in Group 4. LVMI increases with progressive renal function decline. There were linear correlations between LVMI and systolic and diastolic blood pressure (BP), serum creatinine (Scr) and intact parathyroid hormone (PTH) in patients with predialysis CRF and also inverse linear correlations between LVMI and creatinine clearance (Ccr) and hemoglobin. In conclusion, we demonstrate the high prevalence of LVH (87%) in patients with predialysis CRF and concentric hypertrophy (56.5%) was the main pattern of LVH. Several factors such as anemia, systolic and diastolic BP, renal function and PTH influence LVMI.

Key Words : *Kidney failure, chronic; Hypertrophy, left ventricular*

Sung-Kyu Ha, Hong Su Park, Seung Jung Kim, Chong Hoon Park, Dong Su Kim, Hyun Seung Kim

Department of Internal Medicine, Yongdong Severance Hospital, Institute of Kidney Disease, Yonsei University, College of Medicine, Seoul, Korea

Received : May 8, 1998
Accepted : June 15, 1998

Address for correspondence
Sung-Kyu Ha, M.D.
Department of Internal Medicine, Yongdong Severance Hospital, Seoul Young Dong P.O. Box 1217, Seoul, Korea
Tel : +82.2-3497-3313, Fax : +82.2-3463-3882
E-mail : hask1951@yumc.yonsei.ac.kr

INTRODUCTION

Cardiovascular disease is the leading cause of mortality and morbidity in patients on maintenance dialysis, accounting for about 40% of deaths in most registries (1, 2). Clinical manifestations of cardiovascular disease were highly prevalent at the start of dialysis therapy: 14% had coronary artery disease, 19% angina pectoris, 31% cardiac failure, 7% dysrhythmia and 8% peripheral vascular disease (3). Echocardiography provides a non-invasive assessment of left ventricular structure and function and also provide information on both left ventricular geometry and left ventricular contractility. In nonrenal populations, echocardiographic LVH is an adverse prognostic indicator, independent of age, diabetes, hypertension, hyperlipidemia and smoking (4-6). In the Framingham Heart Study, systolic dysfunction, measured by left ventricular fractional shortening was infrequent, but when present was a more powerful predictor of mortality than LVH (7). LVH is detected in approximately 70% of patients at the start of dialysis and it is already well known that LVH is an important determinant of survival in patients with end stage renal disease (ESRD) as well as in patients with normal renal function (3-8). In recent years, echocardiographically detected LVH predicted cardiovascular complications during 4- to 5-year follow-up periods in hypertensive men (9) and in ESRD patients (3, 8). However, whether left ventricular mass measurements identify long-term high risk status in hypertensive men and in patients with ESRD, risk stratification can be further improved by more complete assessment of left ventricular geometry (6). Reports concerning the prevalence and patterns of LVH by a new classification of left ventricular geometry in patients with predialysis CRF are few. In this cross sectional study, we are going to evaluate the prevalence and patterns of LVH by left ventricular geometry in patients with predialysis CRF with variable renal function and analyse the relationship between LVH and various predisposing factors such as anemia, renal function, blood pressure, and secondary

hyperparathyroidism.

PATIENTS AND METHODS

Patients

Sixty-two CRF patients were recruited from our renal clinic with serum creatinine over 2 mg/dl. Patients consist of 29 males and 33 females with mean age of 57.8±15.9. Underlying causes of renal insufficiency were chronic glomerulonephritis 26 (42.0%), diabetic nephropathy 17 (27.4%), hypertensive nephrosclerosis 12 (19.4%), polycystic kidney disease 3 (4.8%), chronic pyelonephritis 1 (1.6%), renal tuberculosis 1 (1.6%) and unknown 2 (3.2 %). To compare the prevalence of LVH, age and degree of hypertension were matched to 42 patients with essential hypertension, who were recruited from our cardiac clinic with normal renal function. Control group consists of 23 males and 19 females with mean age of 55.6±11.4.

Methods

All subjects underwent two-dimensional targeted M-mode echocardiograms recorded in the left lateral decubitus position by Hewlett Packard SONOS 2500 and Vingmed CFM 750. We measured the thickness of the interventricular septum (IVS) at systole and diastole, the thickness of the posterior wall (PWT), and the internal diameter of the left ventricle at end diastole (LVIDD) and systole (LVIDS). Left ventricular mass was calculated using the American Society of Echocardiography cube formula regressed to anatomic validation as described below (10). Left ventricular mass index (LVMI) was calculated by dividing the left ventricular mass by body surface area (BSA); LVMI=LV mass (g)/BSA (m^2). Left ventricular hypertrophy (LVH) was defined in absolute terms as more than 131 g/m^2 in men and more than 100 g/m^2 in women (4,11). Left ventricular ejection fraction (LVEF) and fractional shortening (FS) were calculated by the formula described below. Further characterization of LVH into concentric and eccentric hypertrophy was dependent on measurements of relative wall thickness according to American Society of Echocardiography criteria. Concentric hypertrophy was present if the RWT was equal or greater than 0.45 in the presence of LVH and eccentric hypertrophy was present if the RWT was less than 0.45 in the presence of LVH; concentric remodelling was present if the RWT was equal or greater than 0.45 in the absence of LVH. We classified the patients to 4 groups (Group 1: normal, Group 2: concentric remodelling, Group 3: concentric hypertrophy, Group 4: eccentric hypertrophy).

$$\text{LV mass (g)} = 0.8\,\{1.04\times[(\text{LVIDD}+\text{IVS}+\text{PWT})^3-(\text{LVIDD})^3]\}+0.6\ \text{g}$$

$$\text{LV mass index (LVMI)} = \text{LV mass (g)/BSA}\ (m^2)$$

$$\text{LVEF}\ (\%) = \frac{(\text{LVIDD})^2-(\text{LVIDS})^2}{(\text{LVIDD})^2}\times 100$$

$$\text{FS}\ (\%) = [(\text{LVIDD} - \text{LVIDS})/\text{LVIDD}]\times 100$$

$$\text{RWT} = [(2\times\text{PWT})/\text{LVIDD}]$$

Blood pressure was measured in the supine position after 5 minutes of rest in the out patient clinic. The mean of the three blood pressure determinations obtained on the day of echocardiogram was reported. Hypertension was defined as a mean arterial pressure greater than 105 mmHg or systolic and diastolic pressure greater than 140/90 mmHg, respectively. Fasting laboratory determinations of hemoglobin, intact PTH, and serum creatinine (Scr) were obtained within 1 week of the echocardiography. Creatinine clearance (Ccr) was calculated by the Gault-Cockcroft formula described below (12).

$$\text{Ccr (males)} = (140-\text{age})\times\text{weight (kg)}/72\times\text{serum creatinine (mg/dl)}$$

$$\text{Ccr (females)} = \text{Ccr (males)}\times 0.85$$

Statistical analysis

All data were expressed as mean±SD. Student's t-test, Kruskall-Wallis 1-way ANOVA, Pearson's correlation analysis were used. All tests were considered significant if they met the $p<0.05$ levels.

RESULTS

Clincal characteristics of the hypertensive control and predialysis CRF group showed at Table 1. There were no significant differences between the hypertensive control and predialysis CRF group in the aspects of age, sex, body surface area, and systolic and diastolic blood pressure levels. Various echocardiographic parameters such as, LVMI, RWT, and LVIDD were higher in the predialysis CRF group compared to the hypertensive control. On the other hand, LVEF and FS were lower significantly in the predialysis CRF group (Table 2). The prevalence of LVH in the predialysis CRF group was 87% of patients whereas that of LVH in the hypertensive control was 50%. There were statistically significant differences in the prevalence of LVH between the two groups. Patterns of LVH in the hypertensive control were as follows; Group 1 (40.5

Table 1. Clinical characteristics of the hypertensive control and predialysis CRF patients

	Hypertension patients	CRF patients	p value
Number of patients	42	62	-
Age (years)	55.6±11.4	57.8±15.9	NS
Sex (M:F)	23:19	29:33	NS
BSA (m^2)	1.70±0.18	1.64±0.17	NS
BMI (kg/m^2)	24.2±2.7	22.9±3.6	NS
Systolic BP (mmHg)	154±12	151±18	NS
Diastolic BP (mmHg)	93±7	92±9	NS
Scr (mg/dl)	0.9±0.2	5.9±2.9	<0.05
Ccr (ml/mim)	91.4±20.1	16.1±11.7	<0.05
Hemoglobin (g/dl)	14.1±1.3	8.6±1.5	<0.05
Hematocrit (%)	41.4±3.9	25.6±4.1	<0.05
Intact PTH (pg/ml)	-	190±125	-

CRF, chronic renal failure; BSA, body surface area; BMI, body mass index; BP, blood pressure; Scr, serum creatinine; Ccr, creatinine clearance; PTH, parathyroid hormone.
Data are expressed as mean±SD (NS: statistically not significant).

Table 2. M-mode echocardiographic data in patients with hypertensive control and predialysis CRF

	Hypertension patients	CRF patients	p value
LVMI (g/m^2)	124.9±42.4	165.8±43.2	<0.05
LVIDD (mm)	48.6±4.5	52.6±6.6	<0.05
LVIDS (mm)	29.4±4.2	36.4±7.8	<0.05
IVS-D (mm)	11.3±2.6	12.3±2.8	NS
IVS-S (mm)	15.9±3.1	15.8±3.7	NS
PW-D (mm)	11.3±2.5	12.6±2.3	<0.05
PW-S (mm)	16.5±2.9	17.3±2.3	NS
RWT	0.467±0.100	0.488±0.106	NS
EF (%)	63.0±7.8	51.8±12.5	<0.05
FS	0.40±0.06	0.31±0.09	<0.05

CRF, chronic renal failure; LVMI, left ventricular mass index; LVIDD & LVIDS, internal diameter of LV at diastole & systole; IVS-D & IVS-S, thickness of the ventricular septum at diastole & systole; PW-D & PW-S, thickness of posterior wall at diastole & systole; RWT, relative wall thickness; EF, ejection fraction; FS, fractional shortening.
Data are expressed as mean±SD (NS: statistically not significant).

%), Group 2 (9.5%), Group 3 (40.5%), and Group 4 (9.5%). Patterns of LVH in the predialysis CRF group were as follows; Group 1 (6.5%), Group 2 (6.5%), Group 3 (56.5%), and Group 4 (30.5%). Figure 1 showed distributions of patients in the aspects of LVH pattern between the two groups. In both groups, the most popular pattern was concentric LVH and in the predialysis CRF group, concentric and eccentric LVH increased significantly compared to the hypertensive control. In the predialysis CRF group, we compared the clinical characteristics of the patients with or without LVH (Table 3). There were no significant differences in the aspects of age, sex, and BSA between the two groups. However, systolic and diastolic BP and intact PTH were significantly higher in the patients group with LVH compared to without. We also compared the clinical characteristics and echocardiographic variables of the patients with severe renal functional impairment (Ccr≥20 ml/min) or without (Ccr<

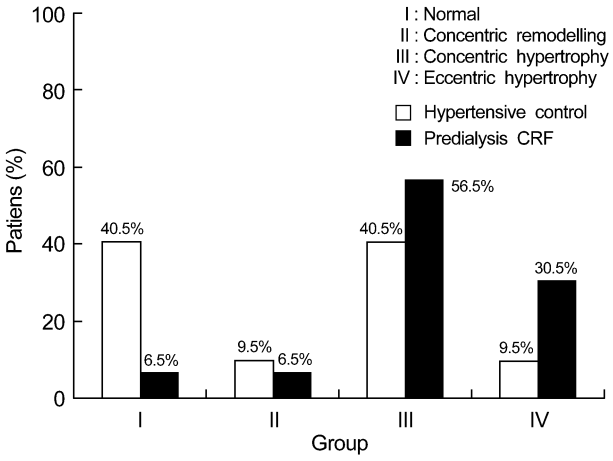

Fig. 1. Patterns of LVH in the Hypertensive control and Predialysis CRF patients. LVH, left ventricular hypertrophy; CRF, chronic renal failure.

Table 3. Comparison of clinical characteristics between those with and without LVH in predialysis CRF patients

	LVH (−)	LVH (+)	p value
Number of patients	8	54	-
Age (years)	64.5±16.4	56.9±15.8	NS
Sex (M:F)	3:5	26:28	NS
BSA (m^2)	1.64±0.19	1.64±0.17	NS
BMI (kg/m^2)	24.3±5.3	22.7±3.3	NS
Systolic BP (mmHg)	133±14	153±18	<0.05
Diastolic BP (mmHg)	82±8	94±8	<0.05
Scr (mg/dl)	3.5±1.1	6.5±2.7	<0.05
Ccr (ml/mim)	28.3±8.1	14.3±11.1	<0.05
Hemoglobin (g/dl)	8.9±1.2	8.6±1.6	NS
Hematocrit (%)	25.6±3.5	25.6±4.2	NS
Intact PTH (pg/ml)	48.6±14.1	203.5±122.9	<0.05

LVH, left ventricular hypertrophy; CRF, chronic renal failure; BSA, body surface area; BMI, body mass index; BP, blood pressure; Scr, serum creatinine; Ccr, creatinine clearance; PTH, parathyroid hormone.
Data are expressed as mean±SD (NS: statistically not significant).

Table 4. Severity of renal dysfunction and various clinical and echocardiographic variables in predialysis CRF patients

	Ccr ≥20 ml/min	Ccr <20 ml/min	p value
Number of patients	16	46	-
Age (years)	59.8±17.6	57.2±15.5	NS
Sex (M:F)	6:10	23:23	NS
Systolic BP (mmHg)	137±17	155±17	<0.05
Diastolic BP (mmHg)	86±8	95±9	<0.05
Hemoglobin (g/dl)	9.4±1.5	8.4±1.4	<0.05
Intact PTH (pg/ml)	38.9±20.4	204.1±121.6	<0.05
LVMI (g/m^2)	131.6±37.7	177.8±38.6	<0.05
LVIDD (mm)	52.1±7.8	52.7±6.3	NS
IVS-D (mm)	10.7±2.3	12.9±2.7	<0.05
PW-D (mm)	10.9±1.8	13.2±2.1	<0.05
RWT	0.43±0.12	0.51±0.10	<0.05
EF (%)	56.3±7.9	50.2±13.4	<0.05
FS	0.34±0.06	0.30±0.10	NS

CRF, chronic renal failure; Ccr, creatinine clearance; BP, blood pressure; PTH, parathyroid hormone; LVMI, left ventricular mass index; LVIDD, internal diameter of LV at diastole; IVS-D, thickness of the ventricular septum at diastole; PW-D, thickness of posterior wall at diastole; RWT, relative wall thickness; EF, ejection fraction; FS, fractional shortening.
Data are expressed as mean±SD (NS: statistically not significant).

Table 5. Correlations between LVMI and various clinical parameters in patients with predialysis CRF

	Correlation coefficient with LVMI
Age	0.1164
Duration of HiBP	0.1665
Systolic BP	0.3803*
Diastolic BP	0.3881*
Scr	0.5320*
Ccr	-0.4294*
Hemoglobin	-0.2834*
Intact PTH	0.4452*

LVMI, left ventricular mass index; CRF, chronic renal failure; HiBP, high blood pressure; Scr, serum creatinine; Ccr, creatinine clearance; PTH, parathyroid hormone.
* means $p<0.05$.

20 ml/min) (Table 4). LVMI increases with progressive renal function decline (177.8 g/m^2 of patients with Ccr< 20 ml/min vs 131.6 g/m^2 of patients with Ccr≥20 ml/min, $p<0.05$). The relationship between LVMI and various clinical parameters showed that there were linear correlations between LVMI and systolic and diastolic BP, Scr and intact PTH in patients with predialysis CRF (LVMI vs systolic BP $r=0.38$, $p<0.05$, LVMI vs diastolic BP $r=0.39$, $p<0.05$, LVMI vs Scr $r=0.53$, $p<0.05$, LVMI vs intact PTH $r=0.45$, $p<0.05$). There were also inverse linear correlations between LVMI and Ccr and hemoglobin (Hb) (LVMI vs Ccr $r=-0.43$, $p<0.05$, LVMI vs Hb $r=-0.28$, $p<0.05$) (Table 5, Fig. 2-4).

DISCUSSION

We have found that there was a very high prevalence of LVH (87.0%) in patients with predialysis chronic renal

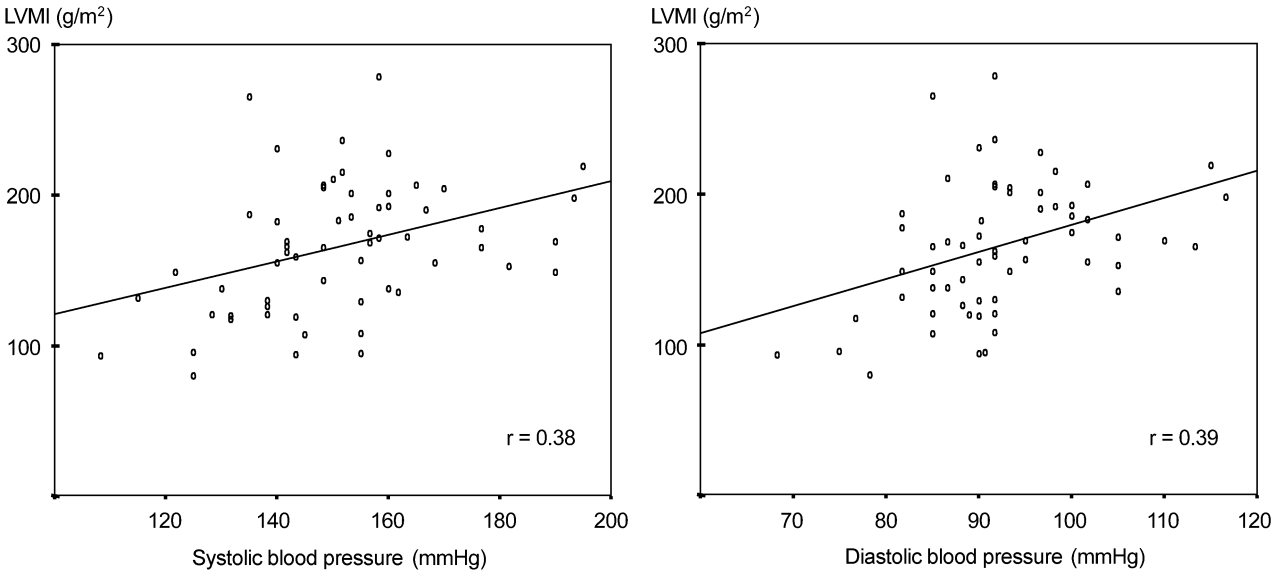

Fig. 2. Linear correlation between left ventricular mass index (LVMI) and blood pressure.

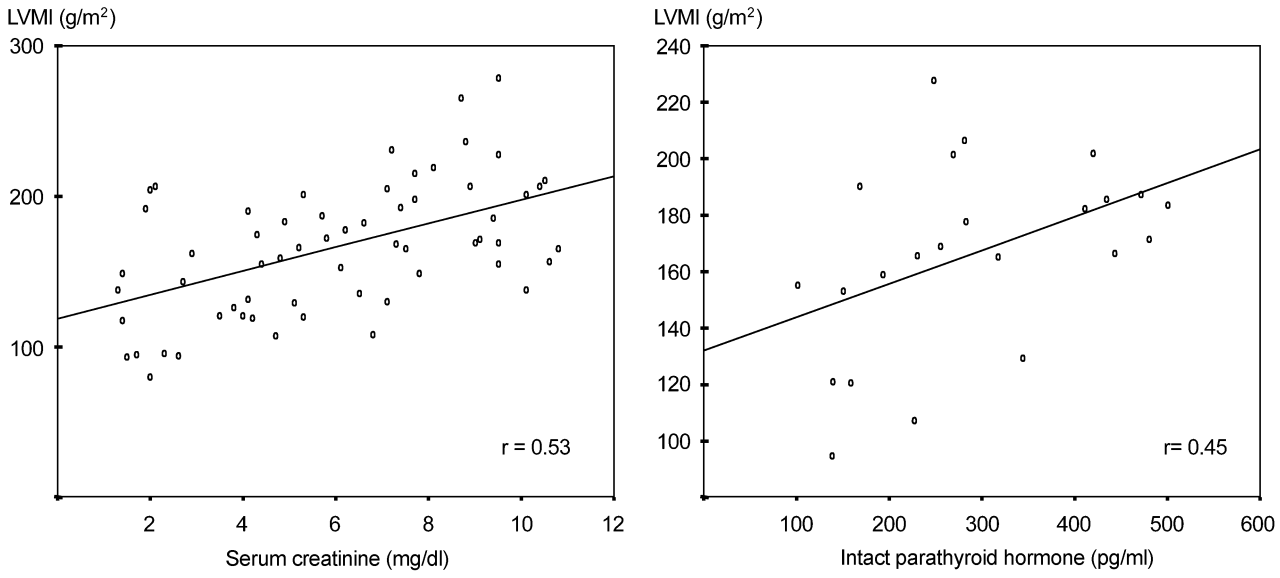

Fig. 3. Linear correlation between left ventricular mass index (LVMI) and serum creatinine (Scr), intact parathyroid hormone (PTH).

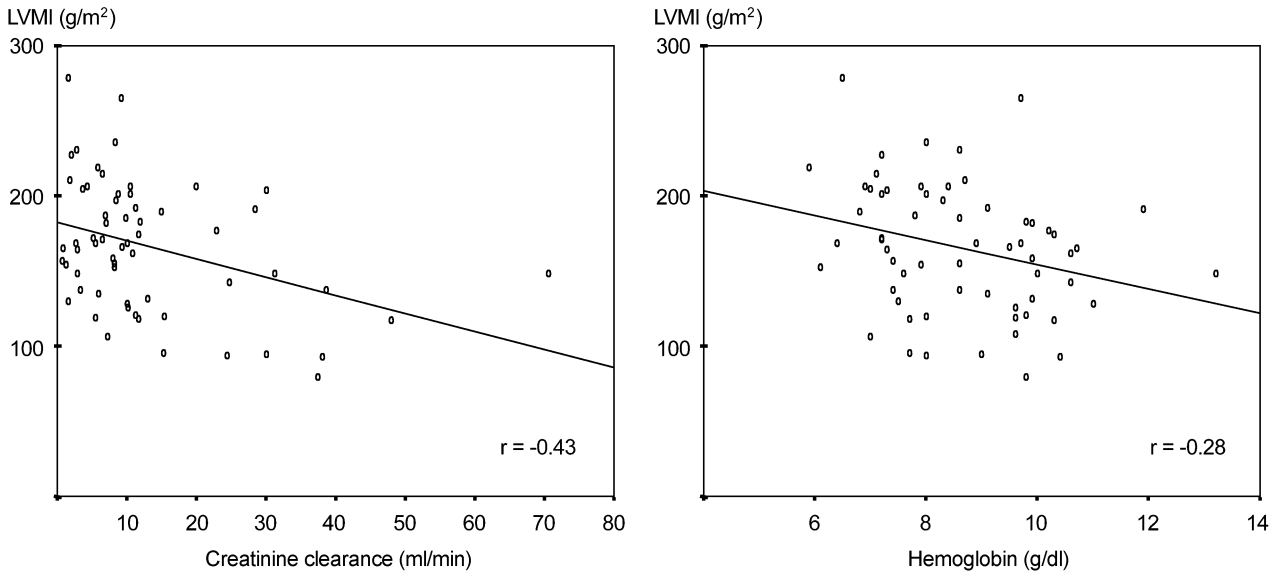

Fig. 4. Inverse linear correlation between left ventricular mass index (LVMI) and creatinine clearance (Ccr), hemoglobin (Hb).

failure. In the Framingham Heart Study, the prevalence of LVH was 17% in the normal population and a higher LV mass predicted a higher incidence of clinical events, including death attributable to cardiovascular disease (4). In recent years, echocardiographically detected LVH predicted cardiovascular complications during 4- to 5-year follow-up periods in hypertensive men (9), in healthy members of the general population (4), and in patients with predialysis CRF and ESRD (3, 13-15). However, it is questionable whether left ventricular mass measurements can identify long-term high risk status in hypertensive men. Risk stratification can be further improved by a more complete assessment of left ventricular geometry (6). In addition to the absolute increase in LV mass, the geometry patterns of left ventricular hypertrophy also may be important. Krumholz et al. tried to determine the prognostic value of left ventricular geometric patterns in the Framingham Heart Study and showed that subjects with concentric hypertrophy had the worst prognosis, followed by those with eccentric hypertrophy, concentric remodelling and normal geometry (16). Koren et al. also showed that patients with normal left ventricular

geometry had the fewest adverse outcome, and those with concentric hypertrophy had the most adverse outcomes in uncomplicated essential hypertension (6). In considering patterns of left ventricular geometry, it has been hypothesized that continuous increment of cardiac pressure produced concentric hypertrophy, whereas continuous increment of cardiac volume led to eccentric hypertrophy (17). Recently, Levin et al. reported the prevalence and patterns of LVH through a new classification of left ventricular geometry in patients with predialysis CRF and showed that the main pattern of LVH was eccentric hypertrophy (57.8%) (13). In our patients, the main pattern was concentric hypertrophy (56.5%) and this result differ from Levin et al. (13). However, compared to essential hypertension group, eccentric hypertrophy was more prevalent in patients with predialysis CRF. These results suggest that patterns of LVH may be affected by hemodialysis per se or other factors related to progressive deterioration of renal function. We have described the relationship between the presence of LVMI and anemia, systolic and diastolic BP, impaired renal function and increased PTH level in this predialysis CRF patients. In regression analysis, serum creatinine had the strongest linear correlation with the LVMI, followed by level of intact PTH, systolic and diastolic BP. And also, creatinine clearance had the strongest negative linear correlation with the LVMI, followed by level of hemoglobin. The progressive decrease of renal function is consistently associated with LVMI (13). It is important to make an intervention to decrease LVMI before severe declining renal function. Blood pressure is also associated with LVH in studies in the general (18) and CRF populations (3, 13). Our results concur with those of similar studies in predialysis patients (13), as well as studies of dialysis populations (3). Anemia has been consistently associated with LVH in the ESRD populations (19, 20), and the results of this study also concur with those in the literature. In general, anemia leads to an increase in cardiac work load due to relative tissue ischemia, which subsequently leads to the development of LVH. We have demonstrated the relationship between intact PTH level and LVMI. Previous studies have inconsistently demonstrated the relationship between intact PTH level and LVMI (13, 19, 21). To study a larger sample and serial measurements over a longer length of time may be needed to clarify the true relationship between intact PTH level and LVMI.

In summary, there was a high prevalence of LVH (87 %) by a left ventricular geometry in patients with predialysis CRF and concentric hypertrophy (56.5%) was the main pattern of LVH. Several factors such as anemia, systolic and diastolic BP, renal function and PTH might influence LVMI. Further studies should focus on interventions aimed at attenuating the impact of these factors related to progressive declining renal function.

REFERENCES

1. US Renal Data System. *USRDS 1994 annual report. Bethesda, Maryland: National Institute of Diabetes and Digestive and Kidney Disease, 1994.*
2. Canadian Organ Replacement Register. *1992 annual report. Canadian Institute for health information, Don Mills, Ontario, March 1994.*
3. Foley RN, Parfrey PS, Harnett JD, Kent GM, Martin CJ, Murray DC, Barre PE. *Clinical and echocardiographic disease in patients starting end-stage renal disease therapy. Kidney Int 1995; 47: 186-92.*
4. Levy D, Garrison RJ, Savage DD, Kannel WR, Castelli WP. *Prognostic implications of echocardiographically determined left ventricular mass in the Farmingham Heart Study. N Engl J Med 1990; 322: 1561-6.*
5. Ghali JK, Liao Y, Simmons B, Castaner A, Cao G, Cooper RS. *The prognostic role of left ventricular hypertrophy in patients with or without coronary artery disease. Ann Intern Med 1992; 117: 831-6.*
6. Koren MJ, Devereux RB, Casale PN, Savage DD, Laragh JH. *Relation of left ventricular mass and geometry to morbidity and mortality in uncomplicated essential hypertension. Ann Intern Med 1991; 114: 345-52.*
7. Lauer MJ, Evans JC, Levy D. *Prognostic implications of subclinical left ventricular dilatation in men free of overt cardiovascular disease (The Framingham Heart Study). Am J Cardiol 1992; 70: 1180-4.*
8. Silberberg JS, Barre P, Prichard S, Sniderman AD. *Impact of left ventricular hypertrophy on survival in end-stage renal disease. Kidney Int 1989; 36: 286-90.*
9. Casale PN, Devereux RB, Milner M, Zullo G, Harshfield GA, Pickering TG, Laragh JH. *Value of echocardiographic measurement of left ventricular mass in predicting cardiovascular morbid events in hypertensive men. Ann Intern Med 1986; 105: 173-8.*
10. Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sach I, Reichek N. *Echocardiographic assessment of left ventricular hypertrophy; Comparison to necropsy findings. Am J Cardiol 1986; 57: 450-8.*
11. Levy D, Savage DD, Garrison RJ, Anderson KM, Kannel WB, Castelli WP. *Echocardiographic criteria for left ventricular hypertrophy: The Framingham Heart Study. Am J Cardiol 1987; 59: 956-60.*
12. Cockroft DW, Gault MH. *Prediction of creatinine clearance from serum creatinine. Nephron 1976; 16: 31-41.*
13. Levin A, Singer J, Thompson CR, Ross H, Lewis M. *Prevalent left ventricular hypertrophy in the predialysis population: Identifying opportunities for intervention. Am J Kidney Dis 1996; 27: 347-54.*

14. Covic A, Goldsmith DJA, Georgescu G, Venning MC, Ackrill P. *Echocardiographic findings in long-term, long-hour hemodialysis patients. Clin Nephrol 1996; 45: 104-10.*
15. Harnett JD, Parfrey PS, Griffiths SM, Gault MH, Barre P, Guttmann RD. *Left ventricular hypertrophy in end-stage renal disease. Nephron 1988; 48: 107-15.*
16. Krumholz HM, Larson M, Levy D. *Prognosis of left ventricular geometric patterns in the Framingham Heart Study. J Am Coll Cardiol 1995; 25: 879-84.*
17. Grossman W, Jones D, McLaurin LP. *Wall stress and patterns of hypertrophy in the human left ventricle. J Clin Invest 1975; 56: 56-64.*
18. Deveureux RB, Pickering TG, Alderman MH, Chien S, Borer JS, Laragh JH. *Left ventricular hypertrophy in hypertension: Prevalence and relationship to pathophysiologic variables. Hypertension 1987; 9(suppl 2): 53-60.*
19. Harnett JD, Kent GM, Barre PE, Taylor R, Parfrey PS. *Risk factors for the development of left ventricular hypertrophy in a prospectively followed cohort of dialysis patients. J Am Soc Nephrol 1994; 4: 1486-90.*
20. Sniderman AD, Silberberg JS, Prichard S, Barre PE. *Anemia and left ventricular function in end stage renal disease. In: Parfrey JD, ed. Cardiac dysfunction in chronic uremia. Boston: Kluwer Academic, 1992: 161-71.*
21. London G, De Vernejoul MC, Fabiani F. *Secondary hyperparathyroidism and cardiac hypertrophy in hemodialysis patients. Kideny Int 1987; 32: 900-7.*