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Changes in Echocardiographic Parameters According to the Rate of Residual Renal Function Decline in Incident Peritoneal Dialysis Patients

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Abstract: Residual renal function (RRF) is associated with left ventricular (LV) hypertrophy as well as all-cause and cardiovascular (CV) mortality in patients with end-stage renal disease. However, no studies have yet examined the serial changes in echocardiographic findings according to the rate of RRF decline in incident dialysis patients.

A total of 81 patients who started peritoneal dialysis (PD) between 2005 and 2012 at Yonsei University Health System, Seoul, South Korea, and who underwent baseline and follow-up echocardiography within the first year of PD were recruited. Patients were dichotomized into ''faster'' and ''slower'' RRF decline groups according to the median values of RRF decline slope (-1.60 mL/min/y/1.73 m^2).

Baseline RRF and echocardiographic parameters were comparable between the 2 groups. During the first year of PD, there were no significant changes in LV end-diastolic volume index (LVEDVI), left atrial volume index (LAVI), or LV mass index (LVMI) in the ''faster'' RRT decline group, while these indices decreased in the ''slower'' RRT decline group. The rate of RRF decline was a significant determinant of 1-year changes in LVEDVI, LAVI, and LVMI. The linear mixed model further confirmed that there were significant differences in the changes in LVEDVI, LAVI, and LVMI between the 2 groups ($P = 0.047$, 0.048, and 0.001, respectively). During a mean follow-up duration of 31.9 months, 4 (4.9%) patients died. Compared with the ''slower'' RRF decline group, CV composite (20.29/100 vs 7.18/100 patient-years [PY], $P = 0.098$), technique failure (18.80/100 vs 4.19/100 PY, $P = 0.006$), and PD peritonitis (15.73/100 vs 4.95/100 PY, $P = 0.064$) developed more frequently in patients with ''faster'' RRF decline rate. On multivariate Cox regression analysis, patients with ''faster'' RRF decline rate showed 4.82-, 4.44-, and 7.37-fold higher risks, respectively, for each clinical outcome.

Preservation of RRF is important for conserving cardiac performance, resulting in an improvement in clinical outcomes of incident PD patients.

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Abbreviations: BSA = body surface area, CAD = coronary artery disease, CHF = congestive heart failure, CV = cardiovascular, DM = diabetes mellitus, ESRD = end-stage renal disease, HbA1c = hemoglobin A1c, HD = hemodialysis, hs-CRP = high-sensitivity C-reactive protein, iPTH = intact parathyroid hormone, IRB = Institutional Review Board, LAE = left atrial enlargement, LAV = left atrial volume, LAVI = left atrial volume index, LMM = linear mixed model, ln hs-CRP = natural log values of high-sensitivity C-reactive protein, LV = left ventricle, LVEDVI = left ventricular end-diastolic volume index, LVESVI = left ventricular end-systolic volume index, LVH = left ventricular hypertrophy, LVMI = left ventricular mass index, PAD = peripheral arterial disease, PD = peritoneal dialysis, PP = pulse pressure, RRF = residual renal function.

INTRODUCTION

Cardiovascular (CV) disease is prevalent and is the most common cause of morbidity and mortality in patients with end-stage renal disease (ESRD). Even though coronary artery disease (CAD) and arrhythmia are not uncommon, left ventricular (LV) hypertrophy (LVH) is the most frequent CV manifestation in these patients.[1] LVH is known to be present in more than 70% of incident ESRD patients and to be a significant independent predictor of CV mortality not only in patients with hypertension but also in those with ESRD.[2–5] Recently, several studies have demonstrated that left atrial volume (LAV) index (LAVI) is also an independent predictor of mortality in patients with ESRD.[6–8]

The importance of residual renal function (RRF) has been highlighted in patients with ESRD. The loss of RRF is closely linked to fluid overload, sodium retention, hypertension, LVH, malnutrition, inflammation, endothelial dysfunction, and anemia, all of which contribute to a higher prevalence of CV disease in dialysis patients.[9,10] In addition, lower RRF was associated with increased morbidity and mortality in ESRD patients receiving hemodialysis (HD) or peritoneal dialysis (PD).[11,12] Especially in PD patients, RRF and fluid removal, but not the dose of PD, were shown to be independent predictors of mortality.[13–17] Even though a number of previous studies

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found that RRF was a favorable factor for clinical outcomes in dialysis patients, most of these studies used only baseline RRF and clarified its impact on all-cause and/or CV mortality.

RRF decreases progressively after the initiation of dialysis, and thus it has been surmised that the impact of the rate of RRF decline rather than baseline RRF is a more important determinant of clinical outcomes of ESRD patients on dialysis. Supporting this point of view, a study by Liao et al[18] revealed that patients with faster RRF decline after PD initiation had worse clinical outcomes, and that the rate of RRF decline rather than baseline RRF was an independent risk factor for technique failure in incident PD patients. The authors also found that the rate of RRF decline was superior to baseline RRF in predicting patient and technique survival in these patients. However, they did not elucidate the mechanism of poor clinical outcomes in patients with a rapid decline of RRF. Since there is a close relationship between RRF and cardiac dysfunction in ESRD patients, the rate of RRF decline may have an effect on the changes in cardiac function, which is closely associated with patient morbidity and mortality. The specifics of this hypothesis have never been explored.

In this study, therefore, we aimed to clarify the changes in echocardiographic findings during the first year of dialysis therapy according to the rate of RRF decline in incident PD patients. Furthermore, we elucidated the prognostic impact of the RRF decline rate on clinical outcome.

PATIENTS AND METHODS

Patients

Initial recruitment for this retrospective cohort study included 148 patients who started PD between January 1, 2005 and July 31, 2012 at Yonsei University Health System, Seoul, South Korea, and who underwent echocardiography, urea kinetic study, and peritoneal equilibration test within 1 month of PD initiation. Among these patients, we excluded those who were younger than 18 years, were anuric (<100 mL/d) at the time of PD initiation, had a history of HD or kidney transplantation prior to PD, had an underlying active malignancy or acute infection, or died within 3 months of PD initiation. Patients who did not receive follow-up echocardiography within the first year of PD treatment were also excluded. Thus, a total of 81 incident PD patients were included in the final analysis.

This study was carried out in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (IRB) of Yonsei University Health System Clinical Trial Center. Since this was a retrospective, medical record–based study and the study subjects were unidentified, the IRB waived the need for written consent from the patients.

Data Collection

Demographic and clinical data, including age, gender, body mass index (calculated as weight/height^2), primary renal disease, comorbidities, and medications, were recorded at the time of PD initiation. CAD was defined as a history of angioplasty, coronary artery bypass grafts, myocardial infarction, or angina, while peripheral arterial disease (PAD) was defined as a history of claudication, ischemic limb loss and/or ulceration, or peripheral revascularization procedure.

Laboratory data were measured from fasting blood samples, which were drawn at 2 hours after the first PD exchange with 1.5% dextrose dialysate on the day when the first urea kinetic study was performed. The following variables were included: hemoglobin, blood urea nitrogen, creatinine, calcium, phosphorus, alkaline phosphatase, intact parathyroid hormone (iPTH), glucose, hemoglobin A1c (HbA1c), albumin, lipid profile, sodium, potassium, bicarbonate, iron profile, N-terminal pro–B-type natriuretic peptide, cardiac troponin T, and high-sensitivity C-reactive protein (hs-CRP). Estimated glomerular filtration rate was calculated using the 4-variable Modification of Diet in Renal Disease study equation.[19] A peritoneal equilibrium test was conducted to determine peritoneal transport characteristics, and dialysis adequacy and RRF were measured within 1 month of beginning PD and every 6 months thereafter. Peritoneal transport characteristics were assessed using equilibration ratios between dialysate and plasma creatinine, which were determined by a standardized peritoneal equilibration test using 2 L 4.25% dextrose dwell with dialysate samples taken at 0, 2, and 4 hours and a plasma sample at 2 hours. According to their 4-hour dialysate-to-plasma creatinine ratios, patients were categorized in 1 of the following 4 peritoneal transport groups: high, high average, low average, or low.[20] Drained whole dialysate and 24-hour urine were collected within 1 day before the peritoneal equilibration test. Creatinine and urea nitrogen were measured in blood, urine, and drained dialysate. To assess dialysis adequacy, weekly Kt/V urea was calculated as the ratio of 24-hour urinary and drained dialysate urea clearance to total body water.[21] RRF was calculated as an average of the 24-hour urine urea and creatinine clearance and was adjusted for body surface area (BSA).[22] Lean body mass was estimated by creatinine kinetics and was divided by dry weight to produce a percent lean body mass.[23]

Echocardiographic Measurements

Echocardiography was performed in the morning with an empty abdomen, based on the imaging protocol recommended by the American Society of Echocardiography using a SONOS 7500 (Philips Ultrasound, Bothell, WA). LV systolic function was estimated by LV ejection fraction using a modified biplane Simpson method from the apical 2-chamber and 4-chamber views. LV mass was determined using the method described by Devereux et al,[24] and the LV mass index (LVMI) was calculated by dividing LV mass by BSA. LVH was defined as LVMI >131 g/m^2 for men and >100 g/m^2 for women.[25] Hypertrophy was considered concentric if LV relative wall thickness was >0.43, and patients with normal LV mass were considered to have normal LV geometry if relative wall thickness was ≤ 0.43 or to have concentric remodeling if relative wall thickness was increased.[26] LAV was assessed using the biplane area–length method from the apical 2- and 4-chamber views and was indexed for BSA. Mitral inflow was assessed with Doppler echocardiography from the apical 4-chamber view (E, A). Pulsed wave tissue Doppler imaging of the septal mitral annulus was also obtained from the apical 4-chamber view (E′, A′). Right ventricular systolic pressure was calculated using the modified Bernoulli equation ($4 \times$ [tricuspid systolic jet]$^2 + 10$ mm Hg).

Outcome Measures

The aim of this study was to clarify time-dependent 1-year changes in echocardiographic parameters according to the rate of RRF decline. Independent factors associated with the RRF decline rate and the impact of RRF decline rate on clinical outcomes, such as all-cause mortality, composite of death or hospitalization, CV composite, infection composite, new-onset CV diseases, technique failure, and PD peritonitis, were also elucidated. A CV event was defined as death or hospitalization from CAD, congestive heart failure (CHF), arrhythmia, pulmonary edema, cerebrovascular disease, or PAD.

Statistical Analysis

Statistical analysis was performed using SPSS for Windows, version 18.0 (SPSS Inc, Chicago, IL). Continuous variables were expressed as mean ± standard deviation or median (interquartile range), while categorical variables were expressed as number (percentage). Normality of distribution was ascertained by the Shapiro–Wilk test. To determine the rate of RRF decline during the first year of PD, linear regression analysis of serial RRF was performed for each patient; the slope was expressed as the regression coefficient. Patients were dichotomized into ''faster'' and ''slower'' RRF decline groups based on the median values of RRF decline slope. Patient demographics, clinical characteristics, laboratory findings, and echocardiographic parameters were compared between the 2 groups

TABLE 1. Baseline Demographic and Clinical Characteristics of Study Patients

Variables	Total (N = 81)	Faster RRF Decline Group (N = 41)	Slower RRF Decline Group (N = 40)	*P*
Age, y	51.5 ± 11.7	51.0 ± 12.4	52.1 ± 11.2	0.702
Sex (male)	40 (49.4%)	23 (56.1%)	17 (42.5%)	0.221
BMI, kg/m^2	23.2 ± 3.5	23.0 ± 2.8	23.4 ± 4.1	0.670
Systolic BP, mm Hg	133.5 ± 21.6	139.7 ± 19.7	127.1 ± 21.9	0.021
Diastolic BP, mm Hg	77.3 ± 12.4	77.5 ± 12.4	77.1 ± 12.6	0.905
Pulse pressure, mm Hg	56.2 ± 16.9	62.2 ± 17.3	50.0 ± 14.1	0.004
Primary cause of end-stage renal disease				0.095
Diabetes	31 (38.3%)	20 (48.8%)	11 (27.5%)	
Hypertension	12 (14.8%)	5 (12.2%)	7 (17.5%)	
Glomerulonephritis	20 (24.7%)	9 (22.0%)	11 (27.5%)	
Interstitial nephritis	3 (3.7%)	2 (4.9%)	1 (2.5%)	
Congenital/hereditary disease	3 (3.7%)	2 (4.9%)	1 (2.5%)	
Others	6 (7.4%)	3 (7.3%)	3 (7.5%)	
Unknown	6 (7.4%)	0 (0.0%)	6 (15.0%)	
Comorbid disease				
Hypertension	73 (90.1%)	38 (92.7%)	35 (87.5%)	0.482
Diabetes	37 (45.7%)	23 (56.1%)	14 (35.0%)	0.057
Chronic lung disease	12 (14.8%)	7 (17.1%)	5 (12.5%)	0.562
CAD	19 (23.5%)	11 (26.8%)	8 (20.0%)	0.468
PAD	3 (3.7%)	2 (4.9%)	1 (2.5%)	0.999
Congestive heart failure	17 (21.0%)	9 (22.0%)	8 (20.0%)	0.829
Arrhythmia	7 (8.6%)	3 (7.3%)	4 (10.0%)	0.712
Cerebrovascular disease	17 (21.0%)	11 (26.8%)	6 (15.0%)	0.191
Connective tissue disease	11 (13.6%)	4 (9.8%)	7 (17.5%)	0.309
Liver disease	1 (1.2%)	0 (0.0%)	1 (2.5%)	0.494
Malignancy	1 (1.2%)	0 (0.0%)	1 (2.5%)	0.494
All CVD*	32 (39.5%)	17 (41.5%)	15 (37.5%)	0.715
Heart disease†	27 (33.3%)	17 (41.5%)	10 (25.0%)	0.116
Modified CCI	5.49 ± 2.47	5.77 ± 2.84	5.20 ± 2.04	0.367
Medications				
RAS blockers	72 (88.9%)	36 (87.8%)	36 (90.0%)	0.999
Diuretics	49 (60.5%)	30 (73.2%)	19 (47.5%)	0.018
β blockers	49 (60.5%)	23 (56.1%)	26 (65.0%)	0.413
CCB	62 (76.5%)	32 (78.0%)	30 (75.0%)	0.746
Nitrate	9 (11.1%)	5 (12.2%)	4 (10.0%)	0.999
Other BP medications	9 (11.1%)	6 (14.6%)	3 (7.5%)	0.482
Statin	25 (30.9%)	11 (26.8%)	14 (35.0%)	0.426
Aspirin	19 (23.5%)	10 (24.4%)	9 (22.5%)	0.841
Plavix	9 (11.1%)	6 (14.6%)	3 (7.5%)	0.482
Vitamin D	25 (30.9%)	12 (29.3%)	13 (32.5%)	0.753
Ca-based P binder	58 (71.6%)	27 (65.9%)	31 (77.5%)	0.245
Non-Ca-based P binder	7 (8.6%)	2 (4.9%)	5 (12.5%)	0.264
ESA	64 (79.0%)	35 (85.4%)	29 (72.5%)	0.155
Iron agents	66 (81.5%)	33 (80.5%)	33 (82.5%)	0.816

BMI = body mass index, BP = blood pressure, Ca = calcium, CAD = coronary artery disease, CCB = calcium channel blocker, CCI = Charlson comorbidity index, CVD = cardiovascular disease, ESA = erythropoiesis-stimulating agent, P = phosphorus, PAD = peripheral artery disease, RAS = renin–angiotensin system, RRF = residual renal function.

* Composite of CAD, PAD, congestive heart failure, arrhythmia, and cerebrovascular disease.

† Composite of CAD, congestive heart failure, and arrhythmia.

TABLE 2. Baseline Laboratory and Peritoneal Dialysis–Related Parameters

Variables	Total (N = 81)	Faster RRF Decline Group (N = 41)	Slower RRF Decline Group (N = 40)	*P*
Hemoglobin, g/dL	10.80 ± 1.68	11.02 ± 1.69	10.58 ± 1.66	0.310
Ca, mg/dL	9.06 ± 0.57	8.98 ± 0.47	9.14 ± 0.66	0.284
P, mg/dL	4.35 ± 0.97	4.40 ± 0.96	4.31 ± 0.99	0.730
Uric acid, mg/dL	6.89 ± 1.59	6.84 ± 1.78	6.94 ± 1.40	0.812
Glucose, mg/dL	109.3 ± 45.4	117.2 ± 56.9	101.1 ± 28.1	0.167
HbA1c, %	6.22 ± 1.20	6.60 ± 1.36	5.90 ± 0.97	0.044
ALP, IU/L	67.9 ± 22.8	66.5 ± 21.5	69.4 ± 24.4	0.626
Protein, g/dL	6.16 ± 0.71	6.22 ± 0.77	6.10 ± 0.66	0.518
Albumin, g/dL	3.40 ± 0.51	3.45 ± 0.59	3.36 ± 0.43	0.507
BUN, mg/dL	49.0 ± 14.5	48.1 ± 14.7	50.0 ± 14.6	0.611
Creatinine, mg/dL	6.84 ± 2.30	6.58 ± 2.02	7.10 ± 2.57	0.378
GFR, mL/min/1.73 m^2	9.47 ± 6.54	9.44 ± 3.94	9.50 ± 8.51	0.974
Sodium, mmol/L	139.1 ± 3.3	138.9 ± 3.7	139.2 ± 3.0	0.730
Potassium, mmol/L	4.00 ± 0.63	3.92 ± 0.65	4.08 ± 0.61	0.344
Chloride, mmol/L	99.5 ± 3.9	99.3 ± 4.0	99.8 ± 3.8	0.569
Bicarbonate, mmol/L	27.2 ± 3.2	27.4 ± 3.5	27.0 ± 2.8	0.640
Intact PTH, pg/mL	164.9 (74.3–290.3)	209.4 (121.9–323.2)	117.8 (43.5–245.3)	0.049
B2MG, mg/L	21.8 ± 8.1	24.6 ± 9.0	19.8 ± 7.0	0.157
Cholesterol, mg/dL	177.9 ± 45.8	179.5 ± 48.2	176.3 ± 43.9	0.788
Triglyceride, mg/dL	131.6 ± 68.3	117.6 ± 52.8	146.6 ± 80.0	0.101
LDL-cholesterol, mg/dL	101.0 ± 39.8	106.2 ± 41.9	95.5 ± 37.4	0.306
HDL-cholesterol, mg/dL	48.1 ± 15.1	47.6 ± 14.4	48.7 ± 16.2	0.769
hs-CRP, mg/dL	4.49 (0.70–19.60)	9.57 (0.93–24.58)	1.37 (0.60–12.07)	0.057
Troponin T, ng/mL	0.034 (0.014–0.115)	0.054 (0.014–0.107)	0.031 (0.013–0.134)	0.741
NT-proBNP, pg/mL	5,278.0 (2,713.0–35,000.0)	11,211.0 (3,004.8–35,000.0)	5,278.0 (1,138.0–35,000.0)	0.740
Serum iron, μg/dL	73.8 ± 40.9	71.6 ± 45.4	76.0 ± 36.4	0.677
TIBC, μg/dL	230.0 ± 47.8	239.3 ± 47.8	220.4 ± 46.6	0.123
TSAT, %	32.3 ± 17.2	30.1 ± 18.7	34.6 ± 15.4	0.316
Ferritin, ng/mL	147.2 (68.9–264.5)	90.7 (54.4–191.6)	211.8 (91.6–374.8)	0.017
Peritoneal dialysis–related parameters				
APD	6 (7.4%)	4 (9.8%)	2 (5.0%)	0.675
Biocompatible solution	6 (7.4%)	4 (9.8%)	2 (5.0%)	0.675
Dialysate volume, mL/d	7,452.8 ± 1,444.2	7,561.9 ± 1,393.8	7,340.0 ± 1,509.8	0.553
Urine volume, mL/d	1,121.2 ± 968.4	1,176.8 ± 1,149.3	1,063.7 ± 753.1	0.652
Total weekly Kt/V urea	2.41 ± 0.62	2.40 ± 0.53	2.43 ± 0.71	0.852
Peritoneal Kt/V urea	1.50 ± 0.43	1.52 ± 0.44	1.48 ± 0.42	0.725
Renal Kt/V urea	0.91 ± 0.66	0.88 ± 0.44	0.95 ± 0.83	0.687
Total weekly CCr, L/wk/1.73 m^2	108.2 ± 36.9	112.6 ± 30.6	103.4 ± 42.6	0.335
Peritoneal CCr, L/wk/1.73 m^2	41.7 ± 10.2	42.9 ± 12.6	40.5 ± 7.0	0.364
Renal CCr, L/wk/1.73 m^2	66.4 ± 37.3	69.7 ± 29.5	62.8 ± 44.5	0.479
RRF, mL/min/1.73 m^2	4.68 ± 2.88	4.83 ± 2.15	4.52 ± 3.53	0.680
RRF slope, mL/min/y/1.73 m^2	−1.91 ± 3.40	−4.29 ± 2.86	0.54 ± 1.79	<0.001
LBM-Cr, kg	40.1 ± 10.1	40.3 ± 10.9	39.9 ± 9.3	0.872
Lean body mass, %	64.8 ± 12.5	65.8 ± 13.8	63.9 ± 11.1	0.561
nPNA, g/kg/d	0.99 ± 0.21	0.97 ± 0.21	1.01 ± 0.22	0.432
D/P creatinine, 4 h	0.6959 ± 0.1027	0.6957 ± 0.1002	0.6962 ± 0.1069	0.984
Groups of peritoneal equilibration test				0.765
High	12 (14.8%)	5 (12.2%)	7 (17.5%)	
High average	44 (54.3%)	23 (56.1%)	21 (52.5%)	
Low average	24 (29.6%)	13 (31.7%)	11 (27.5%)	
Low	1 (1.2%)	0 (0.0%)	1 (2.5%)	

ALP = alkaline phosphatase, APD = automated peritoneal dialysis, B2MG = β_2 microglobulin, BUN = blood urea nitrogen, Ca = calcium, CCr = creatinine clearance, D/P = dialysate/plasma, GFR = glomerular filtration rate, HbA1c = hemoglobin A1c, HDL = high-density lipoprotein, hs-CRP = high-sensitivity C-reactive protein, LBM-Cr = lean body mass estimated by creatinine kinetics, LDL = low-density lipoprotein, nPNA = -protein equivalent of total nitrogen appearance, NT-proBNP = N-terminal pro–B-type natriuretic peptide, P = phosphorus; PTH = parathyroid hormone, RRF = residual renal function, TIBC = total iron-binding capacity, TSAT = transferrin saturation.

TABLE 3. Baseline Values and 1-y Changes in Echocardiographic Parameters

Variables	Total (N = 81)	Faster RRF Decline Group (N = 41)	Slower RRF Decline Group (N = 40)	*P*
Baseline echocardiographic parameters				
LVEDD, mm	50.9 ± 5.3	50.7 ± 4.8	51.1 ± 5.8	0.756
LVESD, mm	34.5 ± 5.7	34.2 ± 5.1	34.8 ± 6.4	0.665
LVEDVI, mL/m^2	74.9 ± 16.7	75.7 ± 16.6	73.7 ± 16.0	0.640
LVESVI, mL/m^2	32.1 ± 16.2	33.2 ± 19.4	31.0 ± 12.5	0.608
LAD, mm	39.4 ± 7.0	38.9 ± 7.2	40.0 ± 6.9	0.570
LAVI, mL/m^2	32.1 ± 13.7	30.2 ± 12.5	33.9 ± 14.9	0.297
Fractional shortening, %	32.5 ± 6.5	32.7 ± 6.5	32.3 ± 6.5	0.791
EF, %	62.3 ± 11.1	62.7 ± 10.9	61.8 ± 11.4	0.777
Inter-ventricular thickness (diastolic phase), mm	11.2 ± 2.0	11.0 ± 2.0	11.3 ± 2.0	0.654
Inter-ventricular thickness (systolic phase), mm	14.1 ± 2.7	13.6 ± 2.4	14.6 ± 2.9	0.155
Posterior wall thickness (diastolic phase), mm	10.9 ± 1.9	10.9 ± 1.9	10.9 ± 1.9	0.898
Posterior wall thickness (systolic phase), mm	14.7 ± 2.4	14.5 ± 2.4	15.0 ± 2.4	0.351
LVMI, g/m^2	131.0 ± 37.1	130.2 ± 37.1	131.8 ± 37.8	0.869
Relative wall thickness	0.435 ± 0.079	0.434 ± 0.083	0.437 ± 0.077	0.893
Geometry of left ventricle				0.941
Normal	17 (21.3%)	9 (22.7%)	8 (19.9%)	
Concentric hypertrophy	31 (37.7%)	15 (35.6%)	16 (39.8%)	
Eccentric hypertrophy	25 (31.1%)	12 (29.1%)	13 (33.2%)	
Concentric remodeling	8 (9.8%)	5 (13.0%)	3 (6.6%)	
E, m/s	0.686 ± 0.219	0.702 ± 0.248	0.670 ± 0.190	0.584
A, m/s	0.788 ± 0.210	0.795 ± 0.236	0.780 ± 0.182	0.792
E′, m/s	0.052 ± 0.021	0.054 ± 0.019	0.051 ± 0.022	0.503
A′, m/s	0.077 ± 0.018	0.079 ± 0.019	0.075 ± 0.017	0.407
S′, m/s	0.067 ± 0.015	0.067 ± 0.014	0.066 ± 0.016	0.774
E/A ratio	0.89 ± 0.33	0.91 ± 0.37	0.87 ± 0.29	0.619
E/E′ ratio	14.4 ± 5.5	14.4 ± 6.4	14.5 ± 4.6	0.921
Diastolic dysfunction				0.594
Normal	11 (13.6%)	4 (9.8%)	7 (17.5%)	
Relaxation abnormality	57 (70.4%)	30 (73.2%)	27 (67.5%)	
Pseudonormalization	13 (16.0%)	6 (14.6%)	7 (17.5%)	
DT, ms	216.9 ± 63.0	214.6 ± 63.2	219.1 ± 63.7	0.787
RVSP, mm Hg	29.0 ± 8.4	29.1 ± 8.0	28.9 ± 8.9	0.942
LAVI, >32 mL/m^2	35 (43.2%)	16 (39.0%)	19 (47.5%)	0.441
EF, <60%	28 (34.6%)	15 (36.6%)	13 (32.5%)	0.699
LVH	56 (69.1%)	27 (65.9%)	29 (72.5%)	0.517
E/E′ (>15)	33 (40.7%)	18 (43.9%)	15 (37.5%)	0.558
1-y changes in echocardiographic parameters				
LVEDD slope, mm/y	−1.21 ± 7.23	1.00 ± 7.89	−3.48 ± 5.76	0.016
LVESD slope, mm/y	−1.01 ± 7.26	0.92 ± 8.18	−3.00 ± 5.63	0.037
LVEDVI slope, mL/m^2/y	−4.61 ± 25.63	3.77 ± 27.68	−13.28 ± 20.34	0.009
LVESVI slope, mL/m^2/y	−1.63 ± 19.67	3.80 ± 23.43	−7.26 ± 12.97	0.029
LAD slope, mm/y	−0.19 ± 7.08	1.03 ± 6.73	−1.46 ± 7.33	0.179
LAVI slope, mL/m^2/y	−2.05 ± 14.55	1.75 ± 11.70	−5.98 ± 16.28	0.037
FS slope, %/y	0.44 ± 9.04	−0.13 ± 10.87	1.02 ± 6.81	0.631
EF slope, %/y	0.78 ± 13.77	−0.23 ± 16.29	1.83 ± 10.77	0.571
LVMI slope, g/m^2/y	−14.50 ± 35.75	−2.58 ± 29.72	−26.83 ± 37.72	0.008
E/A slope, y^{-1}	−0.006 ± 0.594	0.079 ± 0.753	−0.098 ± 0.346	0.279
E/E′ slope, y^{-1}	−2.28 ± 7.05	−1.61 ± 8.64	−2.97 ± 4.96	0.454
DT slope, ms/y	0.46 ± 61.97	0.60 ± 66.43	0.32 ± 58.71	0.987
RVSP slope, mm Hg/y	−4.25 ± 14.04	−2.72 ± 15.22	−5.78 ± 12.92	0.467

DT = deceleration time, EF = ejection fraction, FS = fractional shortening, LAD = left atrial dimension, LAVI = left atrial volume index, LVEDD = left ventricular end-diastolic dimension, LVEDVI = left ventricular end-diastolic volume index, LVESD = left ventricular end-systolic dimension, LVESVI = left ventricular end-systolic volume index, LVH = left ventricular hypertrophy, LVMI = left ventricular mass index, RRF = residual renal function, RVSP = right ventricular systolic pressure.

using Student *t* test or Mann–Whitney *U* test for continuous variables and the χ^2 test for categorical variables. Time-dependent serial changes in echocardiographic parameters (LV end-diastolic volume index [LVEDVI], LAVI, and LVMI) during the first year of PD were compared between the 2 groups using the linear mixed model (LMM), which utilized patient groups, time, and interaction term between patient groups and time as fixed effects. The final adjusted model was chosen on the basis of the Akaike information criterion. In our implementation of the mixed model, subject and intercept were treated as random effects. To determine independent factors associated with the rate of RRF decline, multivariate linear regression analysis was performed. Cumulative survival curves for clinical outcomes were created by the Kaplan–Meier method, and between-group survival was compared by a log-rank test. The independent prognostic power of RRF decline rate for CV composite outcome, technique failure, or PD peritonitis was ascertained by multivariate Cox proportional hazards regression analysis, which included only the variables with *P* value <0.10 on the univariate analysis. *P* values less than 0.05 were considered statistically significant.

RESULTS

Baseline Characteristics

The baseline demographic and clinical characteristics are shown in Table 1. The mean age was 51.5 ± 11.8 years, and 49.4% of patients were males. The most common cause of ESRD was diabetes mellitus (DM, 38.3%), followed by glomerulonephritis (24.7%) and hypertension (14.8%). When patients were dichotomized into 2 groups according to the median value of RRF slope (−1.60 mL/min/y/1.73 m^2), systolic blood pressure, pulse pressure (PP), and the proportion of patients on diuretics were significantly higher in the ''faster'' RRF decline group compared with those in the ''slower'' RRF decline group.

Among laboratory variables, HbA1c and iPTH levels were significantly higher in the ''faster'' RRF decline group compared with those in the ''slower'' RRF decline group, while serum ferritin levels were significantly lower. There was a trend of higher hs-CRP levels in patients with rapid RRF decline compared with those in the ''slower'' RRF decline group, but it did not reach statistical significance (Table 2).

On the other hand, PD-related parameters such as the proportion of patients on automated PD or with biocompatible nonglucose PD solution use, weekly Kt/V urea and creatinine clearance, baseline RRF, and the distribution of peritoneal characteristics were not significantly different between the 2 groups (Table 2). Baseline echocardiographic parameters were also comparable between the 2 groups (Table 3).

One-Year Serial Changes in Echocardiographic Parameters According to the Rate of RRF Decline

On a simple comparison using Student *t* test, there were significant decreases in LVEDVI, LV end-systolic volume index (LVESVI), LAVI, and LVMI during the first year of

TABLE 4. Determining Factors for the Changes in Echocardiographic Parameters, LVEDVI, LAVI, and LVMI, During the First Year of Peritoneal Dialysis (Multivariate Linear Regression Analysis)

	Regression Coefficient	*P*
Slope of LVEDVI		
HbA1c, %	5.056	0.098
Alkaline phosphatase, IU/L	0.128	0.469
Iron supplements	−12.971	0.198
Biocompatible solution	−25.349	0.051
Faster RRF decline group (vs slower RRF decline group)	17.953	0.019
Baseline echocardiographic parameters		
LVEDVI, mL/m^2	−0.452	0.035
Slope of LAVI		
Arrhythmia	11.056	0.107
Sodium, mmol/L	−0.794	0.047
Plavix	8.794	0.046
Faster RRF decline group (vs slower RRF decline group)	8.543	0.006
Baseline echocardiographic parameters		
LAVI, mL/m^2	−0.468	0.005
Ejection fraction, %	0.162	0.283
E/A	−8.465	0.081
Slope of LVMI		
Congestive heart failure	25.960	0.006
Alkaline phosphatase, IU/L	0.401	0.018
Albumin, g/dL	−3.417	0.540
APD (vs CAPD)	7.367	0.621
Faster RRF decline group (vs slower RRF decline group)	21.004	0.005
Baseline echocardiographic parameters		
LVMI, g/m^2	−0.416	<0.001

APD = automated peritoneal dialysis, CAPD = continuous ambulatory peritoneal dialysis, HbA1c = hemoglobin A1c, LAVI = left atrial volume index, LVEDVI = left ventricular end-diastolic volume index, LVMI = left ventricular mass index, RRF = residual renal function.

PD in patients with ''slower'' RRF decline compared with those in the ''faster'' RRF decline group (Table 3). In addition, the rate of RRF decline was a significant independent factor associated with changes in LVEDVI, LAVI, and LVMI on multivariate linear regression analysis (Table 4). Next, we compared the time-dependent 1-year serial changes in echocardiographic parameters between the ''faster'' and ''slower'' RRF decline groups (Table 5; Figure 1; Supplementary Figure 1, http://links.lww.com/MD/A167). LVEDVI and LVMI values were comparable between the 2 groups at baseline and decreased similarly until 6 months. After 6 months, however, patients with ''slower'' RRF decline showed a continuous regression pattern, while these values stopped decreasing in the ''faster'' RRF decline group, resulting in significant differences between the 2 groups at 12 months ($P = 0.045$ and 0.003, respectively). LMM further confirmed that the overall reduction rates of LVEDVI and LVMI were significantly greater in patients with ''slower'' RRF decline compared with those in the ''faster'' RRF decline group, even after adjusting for confounding factors ($P = 0.047$ and 0.001, respectively). LAVI also decreased gradually in the ''slower'' RRF decline group, while it was slightly increased at 6 and 12 months in the ''faster'' RRF decline group, resulting in a significant difference in LMM ($P = 0.048$).

In contrast, the changes in echocardiographic parameters during the first year of PD showed no differences between patients who were grouped by median values of baseline RRF (Supplementary Table 1, http://links.lww.com/MD/A168).

Independent Factors Associated With the Rate of RRF Decline

On multivariate linear regression analysis, natural log values of hs-CRP (Ln hs-CRP) and baseline E/A values were significant independent factors associated with the rate of RRF decline during the first year of PD. After including the 1-year changes in echocardiographic parameters (LVEDVI, LAVI, or LVMI) into the successive models, PP, Ln hs-CRP levels, baseline E/A, and the slope of each echocardiographic parameter were found to be significant determinants of the RRF decline rate. Among 3 variances in cardiac performance, only the changes in LAVI remained statistically significant in the final model (Table 6).

TABLE 5. Time-Dependent Changes in Echocardiographic Parameters During the First Year of PD, According to the Rate of RRF Decline

	Faster RRF Decline Group (N = 41)	Slower RRF Decline Group (N = 40)	*P* (95% CI)
LVEDVI, mL/m^2			
Baseline	75.7 ± 16.6	73.7 ± 16.0	0.640 (−10.503, 6.507)
6-mo	69.9 ± 13.0	67.9 ± 16.9	0.759 (−15.391, 11.388)
12-mo	77.8 ± 30.1	64.5 ± 14.4	0.045 (−26.175, −0.337)
LVEDVI slope, mL/m^2/y	3.77 ± 27.68	−13.28 ± 20.34	0.009 (−29.748, −4.347)
LMM 1			0.027 (−11.664, −0.713)
LMM 2*			0.046 (−10.292, −0.085)
LMM 3†			0.047 (−12.061, −0.106)
LAVI, mL/m^2			
Baseline	30.2 ± 12.5	33.9 ± 14.9	0.297 (−3.331, 10.707)
6-mo	30.5 ± 12.3	31.5 ± 17.6	0.873 (−12.101, 14.140)
12-mo	33.2 ± 16.8	27.7 ± 10.7	0.176 (−13.494, 2.532)
LAVI slope, mL/m^2/y	1.75 ± 11.70	−5.98 ± 16.28	0.037 (−14.971, −0.483)
LMM 1			0.045 (−6.048, −0.065)
LMM 2‡			0.042 (−6.330, −0.126)
LMM 3§			0.048 (−5.596, −0.014)
LVMI, g/m^2			
Baseline	130.2 ± 37.1	131.8 ± 37.8	0.869 (−17.576, 20.757)
6-mo	121.0 ± 41.1	123.7 ± 39.6	0.866 (−30.614, 36.120)
12-mo	129.9 ± 36.0	100.6 ± 29.4	0.003 (−47.831, −10.812)
LVMI slope, g/m^2/y	−2.58 ± 29.72	−26.83 ± 37.72	0.008 (−41.915, −6.572)
LMM 1			0.002 (−19.328, −4.750)
LMM 2‖			0.001 (−17.790, −5.051)
LMM 3¶			0.001 (−17.756, −5.048)

CI = confidence interval, LAVI = left atrial volume index, LMM = linear mixed model, LVEDVI = left ventricular end-diastolic volume index, LVMI = left ventricular mass index, PD = peritoneal dialysis, RRF = residual renal function.

* Adjusted for left ventricular end-diastolic volume index.

† Adjusted for the usage of iron supplements and biocompatible dialysate, serum hemoglobin A1c and alkaline phosphatase levels, and left ventricular end-diastolic volume index.

‡ Adjusted for the usage of Plavix, serum sodium levels, and LAVI.

§ Adjusted for arrhythmia, usage of Plavix, serum sodium levels, LAVI, ejection fraction, and E/A.

‖ Adjusted for congestive heart failure, serum alkaline phosphatase levels, and LVMI.

¶ Adjusted for congestive heart failure, automated peritoneal dialysis, serum alkaline phosphatase and albumin levels, and LVMI.

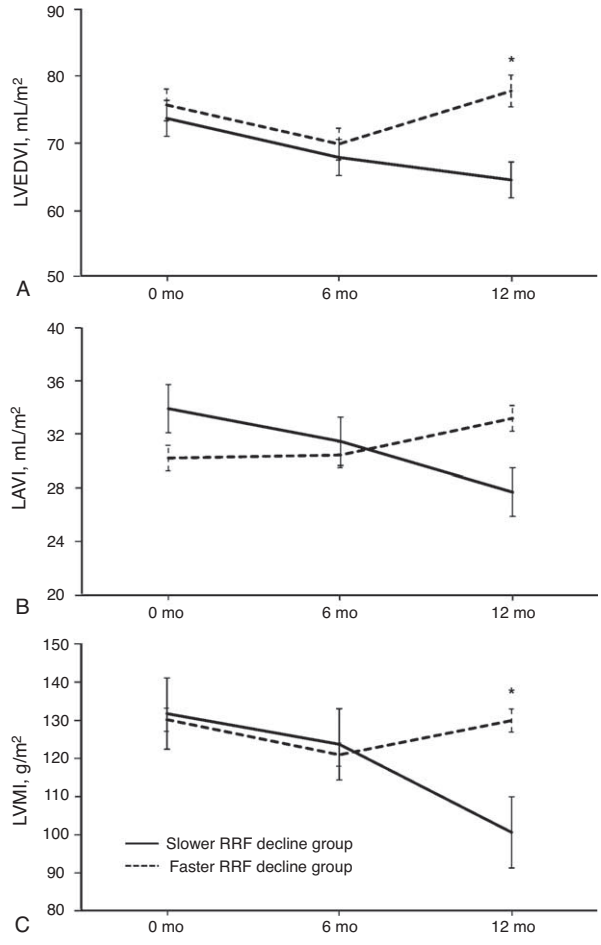

FIGURE 1. Time-dependent serial changes in echocardiographic parameters according to the rate of RRF decline. During the first year of PD, LVEDVI (A), LAVI (B), and LVMI (C) decreased continuously in patients with ''slower'' RRF decline, while no improvement or a slightly deteriorating pattern was observed in the ''faster'' RRF decline group. LAVI = left atrial volume index, LVEDVI = left ventricular end-diastolic volume index, LVMI = left ventricular mass index, PD = peritoneal dialysis, RRF = residual renal function.

Clinical Outcomes According to the Rate of RRF Decline

During a mean follow-up duration of 31.9 months, 4 (4.9%) patients died. The event rates for all-cause mortality, composite of death or hospitalization, infection composite, and new-onset CV disease were not different between the 2 groups. In contrast, compared with patients with ''slower'' RRF decline, the ''faster'' RRF decline group showed a significantly higher rate of technique failure (18.80 vs 4.19 events/100 patient-years [PY], $P = 0.006$). CV composite (20.29 vs 7.18 events/100 PY, $P = 0.098$) and PD peritonitis (15.73 vs 4.95 events/100 PY, $P = 0.064$) also developed more frequently in the ''faster'' RRF decline group, but the differences did not reach statistical significance (Table 7). However, Kaplan–Meier analysis revealed that CV composite, technical failure, and PD peritonitis event-free survivals were significantly higher in the ''slower'' RRF decline group compared with those in the ''faster'' RRF decline group (Figure 2).

Multivariate Cox regression analysis demonstrated that patients with rapid RRF decline had 4.82-, 4.44-, and 7.37-fold higher risks for CV composite outcome ($P = 0.032$), technique failure ($P = 0.031$), and PD peritonitis ($P = 0.017$), respectively. Moreover, the significance of the rate of RRF decline was more powerful than that of baseline RRF values in predicting each clinical outcome (Table 8). However, the significant impact of RRF decline rate on CV composite and technique failure was no longer observed when further adjustments were made with 1-year changes in echocardiographic parameters (Supplementary Table 2, http://links.lww.com/MD/A169).

DISCUSSION

A number of previous studies have shown that lower RRF is associated with increased morbidity and mortality in ESRD patients on HD or PD.[11–17,27] Furthermore, RRF and cardiac function are known to influence each other.[28] Therefore, some changes in echocardiographic findings are expected over time as RRF declines in incident dialysis patients, but this trend has not previously been explored. In the current study, we demonstrate for the first time that slow RRF decline is significantly associated with time-dependent decreases in LVEDVI, LAVI, and LVMI during the first year of PD, indicating an improvement in cardiac morphology and function. Furthermore, a rapid decline in RRF independently predicted adverse clinical outcomes such as CV composite, technique failure, and PD peritonitis.

RRF plays a pivotal role in maintaining sodium and water balance of dialysis patients, and thus loss of RRF leads to chronic volume expansion and hypertension.[9,10] The severity of anemia is also known to correlate with RRF.[29,30] All these factors contribute to the development of LVH and left atrial enlargement (LAE). Therefore, it is a matter of course that LVH and LAE progress as RRF declines, but this trend has not previously been explored in dialysis patients. As expected, the present study found that there were increases in LVEDVI, LVESVI, and LAVI in patients with rapid RRF decline. However, these parameters were relatively decreased in the ''slower'' RRF decline group, which seemed to be partly attributed to an increase in mean RRF in this group. In contrast, LVMI was decreased in both groups even though the reduction of LVMI was significantly greater in patients with ''slower'' RRF decline. We inferred that correction of uremia and hyperparathyroidism rather than improvement in fluid balance and/or anemia contributed to the regression of LVMI in the ''faster'' RRF decline group in spite of a significant decrease in RRF.

Mounting evidence indicates that LVH is a powerful independent predictor of CV mortality in patients with chronic kidney disease and ESRD.[4,5] The change in LVH has also been considered a strong prognostic factor in these patients. A previous prospective study on prevalent HD patients revealed that the rates of LVMI increase were significantly higher in patients with incident CV events than in those without such events, and that CV event-free survival in patients with changes in LVMI below the 25th percentile was significantly higher than in those with changes above the 75th percentile.[2] Similarly, in a cohort study of 153 incident ESRD patients receiving HD, a 10% reduction in LV mass during a mean follow-up duration of 54 months resulted in a 22% decrease in all-cause mortality and a 28% decrease in CV mortality. Furthermore, in that study, LV mass regression was independently associated with improved

TABLE 6. Determining Factors for the Slope of Residual Renal Function

	Model 1		Model 2		Model 3		Model 4		Model 5	
Variables	**Regression Coefficient**	***P***	**Regression Coefficient**	***P***	**Regression Coefficient**	***P***	**Regression Coefficient**	***P***	**Regression Coefficient**	***P***
Sex (female)	1.175	0.127	1.023	0.175	1.136	0.107	0.955	0.196	1.025	0.154
Pulse pressure, mm Hg	−0.034	0.060	−0.034	0.048	−0.035	0.032	−0.037	0.028	−0.038	0.023
Ln hs-CRP, mg/dL	−0.509	0.012	−0.414	0.036	−0.597	0.002	−0.426	0.027	−0.528	0.008
Baseline echocardiographic parameters										
E/A	−3.285	0.006	−3.798	0.001	−4.480	<0.001	−3.346	0.003	−4.171	0.001
1-y changes in echocardiographic parameters										
LVEDVI slope, mL/m^2/y	—	—	−0.031	0.031	—	—	—	—	0.008	0.697
LAVI slope, mL/m^2/y	—	—	—	—	−0.080	0.002	—	—	−0.063	0.039
LVMI slope, g/m^2/y	—	—	—	—	—	—	−0.026	0.010	−0.020	0.139

Model 1: adjusted for demographics (sex and pulse pressure), laboratory findings (Ln hs-CRP), and baseline echocardiographic parameters (E/A). Model 2: Model 1 + LVEDVI slope. Model 3: Model 1 + LAVI slope. Model 4: Model 1 + LVMI slope. Model 5: Model 1 + slope of LVEDVI, LAVI, and LVMI. LAVI = left atrial volume index, Ln hs-CRP = log transformed high-sensitivity C-reactive protein, LVEDVI = left ventricular end-diastolic volume index, LVMI = left ventricular mass index.

patient survival even after adjustment for age, gender, DM, history of CV disease, and all nonspecific CV risk factors.[3] On the other hand, since considerable recent evidence has shown that LAV is a significant risk factor for poor outcome in patients with various CV diseases, such as cardiomyopathy, acute myocardial infarction, and preexisting atrial fibrillation,[31–34] several studies have been conducted and demonstrated that LAV predicts mortality in the HD population on long-term low-salt diets and in ESRD patients with LVH.[6,35] In addition, Tripepi et al[8] found that LAV indexed for height but not crude or BSA-adjusted LAV was independently associated with mortality in ESRD patients on dialysis. Moreover, they showed that changes in LAV predicted incident fatal and nonfatal CV events in dialysis patients, independent of baseline LAV or LV mass.[36] Exclusively in PD patients, Kim et al[7] also demonstrated that LAVI was an independent predictor of all-cause and CV mortality, and that increased LAVI better predicted adverse outcomes than other echocardiographic parameters. Based on these findings, baseline LVH and/or LAV as well as changes in these parameters seem to be important prognostic factors for clinical outcomes in ESRD patients on dialysis.

Since the first study by Maiorca et al,[11] which demonstrated that RRF was significantly higher in patients who survived compared with that in those who died (2.73 ± 2.49 vs 0.33 ± 0.86 mL/min, $P = 0.0005$), and that RRF was an independent predictor of survival in 102 prevalent dialysis patients, many subsequent studies have shown a significant impact of RRF on the clinical outcomes in ESRD patients on HD or PD. The Netherlands Cooperative Study on the Adequacy of Dialysis-2 demonstrated that there was a 56% decrease in relative risk of death ($P < 0.0001$) with an increase of 1/week in renal Kt/V urea in 740 incident HD patients. In that study, the influence of dialysis dose on mortality was found to be significant only in anuric patients.[37] Termorshuizen et al[14] also showed that a 12% reduction in mortality rate ($P = 0.039$) was observed for each mL/min/1.73 m^2 increase in RRF in 413 incident PD patients, and that there was no significant effect of peritoneal creatinine clearance on patient survival, which was consistent with the results of previous studies by Szeto et al[15] and Rocco et al.[16] In contrast to numerous investigations on the association of baseline RRF and clinical outcome in ESRD patients, the impact of the RRF decline rate on clinical outcome

TABLE 7. Comparisons of Clinical Outcomes According to the Rate of RRF Decline

	Faster RRF Decline Group (N = 41)		Slower RRF Decline Group (N = 40)		
	N (%)	**Rates (/100 PY)**	**N (%)**	**Rates (/100 PY)**	***P***
All-cause mortality	3 (7.3)	3.54	1 (2.5)	1.56	0.616
Composite*	34 (82.9)	79.82	31 (77.5)	56.75	0.540
CV composite*	15 (36.6)	20.29	8 (20.0)	7.18	0.098
Infection composite*	18 (43.9)	28.46	14 (35.0)	16.52	0.413
New-onset CV disease	15 (36.6)	20.29	12 (30.0)	12.31	0.530
Technique failure	16 (39.0)	18.80	5 (12.5)	4.19	0.006
PD peritonitis	12 (29.3)	15.73	5 (12.5)	4.95	0.064

CV = cardiovascular, PD = peritoneal dialysis, PY = patient-year, RRF = residual renal function.
* Composite: composite of death or hospitalization.

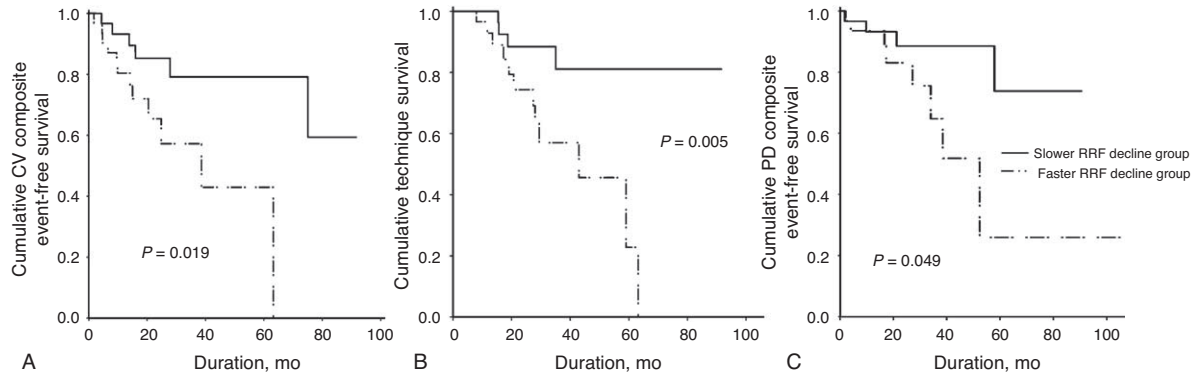

FIGURE 2. Kaplan–Meier curves for CV composite outcome (A), technique failure (B), and PD peritonitis (C). Patients with ''faster'' RRF decline rate (≤ -1.60 mL/min/y/1.73 m^2) showed significantly worse clinical outcomes compared with the ''slower'' RRF decline group. CV = cardiovascular, PD = peritoneal dialysis, RRF = residual renal function.

has been rarely explored in this population. A previous study from the United Kingdom revealed that loss of RRF occurred significantly earlier in nonsurvivors than in survivors (0.37 vs 0.68, $P = 0.02$ at 6 months, 0.19 vs 0.54, $P = 0.01$ at 12 months) despite comparable RRF values at the start of PD treatment.[38] Furthermore, Liao et al[18] observed that patients with fast RRF decline had worse survival and increased risk of technique failure, and that the rate of RRF decline was an independent

TABLE 8. Multivariate Cox Proportional Hazard Regression Analysis for Cardiovascular Composite Outcome, Technique Failure, and PD Peritonitis

Variables	HR	95% CI	*P*
Cardiovascular composite outcome			
Pulse pressure, mm Hg	1.021	0.983–1.062	0.277
Diabetes	5.290	1.165–24.016	0.031
Ln hs-CRP, mg/dL	1.309	0.513–1.136	0.184
Lean body mass, %	0.980	0.924–1.039	0.491
nPNA, g/kg/d	0.823	0.066–10.197	0.879
Baseline RRF $\leq$ median (vs >median)	3.777	1.013–14.082	0.048
Faster RRF decline group (vs slower RRF decline group)	4.815	1.147–20.218	0.032
Baseline echocardiographic parameters			
EF $\leq$ 60% (vs >60%)	3.207	0.948–10.845	0.061
Technique failure			
Albumin, g/dL	0.529	0.177–1.577	0.253
Cholesterol, mg/dL	0.991	0.976–1.006	0.245
Vitamin D	0.279	0.054–1.428	0.125
Baseline RRF $\leq$ median (vs >median)	1.896	0.455–7.904	0.380
Faster RRF decline group (vs slower RRF decline group)	4.439	1.147–17.179	0.031
Baseline echocardiographic parameters			
Diastolic dysfunction			
Relaxation abnormality versus normal	4.344	0.347–54.398	0.255
Pseudonormalization versus normal	20.125	1.118–236.288	0.042
PD peritonitis			
Sex (female)	10.079	1.421–71.472	0.021
Charlson comorbidity index	1.303	0.876–1.938	0.191
Glucose, mg/dL	1.018	0.998–1.038	0.081
Sodium, mmol/L	0.858	0.699–1.054	0.144
Ln hs-CRP, mg/dL	1.144	0.592–1.776	0.566
Baseline RRF $\leq$ median (vs >median)	8.507	1.279–56.604	0.027
Faster RRF decline group (vs slower RRF decline group)	7.368	1.427–38.041	0.017
Baseline echocardiographic parameters			
Left ventricular hypertrophy	19.407	1.477–255.046	0.024

CI = confidence interval, EF = ejection fraction, HR = hazard ratio, Ln hs-CRP = log transformed high-sensitivity C-reactive protein, nPNA = -protein equivalent of total nitrogen appearance, PD = peritoneal dialysis, RRF = residual renal function.

factor associated with patient and technique survival and was a more powerful prognostic factor than basal RRF. However, these 2 studies did not clearly elucidate the mechanism of adverse clinical outcomes due to faster RRF decline. In this study, we demonstrated that CV composite was significantly worse in the ''faster'' RRF decline group compared with that in the ''slower'' RRF decline group, which was consistent with the results of aforementioned studies. In addition, there were significant differences in the changes in LVEDVI, LVESVI, LAVI, and LVMI between patients with ''faster'' and ''slower'' RRF decline, indicating deterioration or less improvement of cardiac performance in the ''faster'' RRF decline group. Moreover, the significant impact of the RRF decline rate on CV composite was no longer observed when further adjustments were made with 1-year changes in echocardiographic parameters. These findings suggest that the influence of RRF decline on CV composite was in part attributed to the changes in cardiac performance in incident PD patients.

On the other hand, technical survival and peritonitis event-free survival were significantly higher in our patients with ''slower'' RRF decline. An observational study by Szeto et al[27] found that PD patients with RRF had significantly lower peritonitis rates compared with dialysis-dependent PD patients (1 episode per 44.4 vs 13.6 patient-months, $P < 0.05$). Perez Fontan et al[39] also showed that lower RRF at the start of PD was an independent risk factor for at least 1 episode of peritonitis and its related mortality in 565 PD patients. Furthermore, a study by Han et al[40] revealed that time to first peritonitis episode was significantly longer and peritonitis rate was significantly lower in patients with RRF > 5 mL/min/1.73 m^2 compared with in those with RRF ≤ 5 mL/min/1.73 m^2 (0.24 vs 0.57 episode per PY, $P < 0.001$). The exact underlying mechanisms by which RRF impacts technical failure and peritonitis are not clear, but Wang et al[41] postulated that loss of RRF may compromise the general condition and immunocompetence of PD patients. Since peritonitis is the principal cause of technical failure in PD patients,[42] lower peritonitis rate may partly account for a significantly higher technical survival rate in our ''slower'' RRF decline group.

Previous studies have demonstrated that high transporter, DM, CHF, hypotension, extracellular fluid volume depletion, use of diuretics, and peritonitis are associated with the loss of RRF in PD patients,[9] although controversy exists concerning the role of diuretics in RRF.[18,43] In the current study, the proportions of DM patients and patients on diuretics were higher in the ''faster'' RRF decline group, but DM and diuretics usage were not independent predictors of RRF decline rates on multivariate analysis. Instead, hs-CRP levels, baseline E/A, and changes in LAVI were significant determinants of the rate of RRF decline. Several previous studies have found that high baseline LAVI is an independent risk factor for a rapid decline in RRF in incident PD patients.[44,45] It is true that chronic heart failure can provoke renal hypoperfusion and increase renal vascular resistance, which in turn results in the impairment of renal function. In addition, atrial stretch facilitates neurohormonal activation, including the production of vasoconstrictive mediators, leading to further aggravation of renal dysfunction.[28] In diastolic dysfunction, moreover, mild volume changes in cardiac filling may induce a significant decrease in cardiac output and systemic hypotension, resulting in reduced renal perfusion.[46] Since left atrial size is regarded as a more stable indicator of the duration and severity of diastolic dysfunction than any other echocardiographic parameter,[47] it is surmised that LV diastolic dysfunction and LAE can influence the decline in RRF. hs-CRP level, an indicator of inflammation, has been shown to be significantly associated with cardiac dysfunction, which may contribute to a more rapid decline in RRF.[48] Furthermore, systemic inflammation-induced cytokines may have a direct deleterious effect on renal perfusion.[49]

Several shortcomings of the present study should be discussed. First, since this was a retrospective medical record–based study, the observational nature could limit the causational interpretation of our study results. We cannot determine conclusively if RRF decline influenced the changes in echocardiographic parameters, or vice versa. However, multivariate analysis revealed that the RRF decline rate was a significant independent factor associated with changes in LVEDVI, LAVI, and LVMI, and that the changes in these echocardiographic parameters were significant independent predictors of the rate of RRF decline, suggesting an interrelationship between RRF and cardiac performance. Second, only a small number of Korean incident PD patients from a single center were included. Therefore, the association between the rate of decline in RRF and the changes in echocardiographic parameters may not be generalizable to other populations. Third, the mortality and event rates were relatively low compared with those of previous studies on Western ESRD patients, but they were comparable to those of Japanese ESRD patients.[50] A small number of patients and events and a relatively short follow-up duration may limit the power of the statistical analysis in this study. Fourth, we excluded patients who did not receive follow-up echocardiography more than once during the first year of PD, and thus selection bias may have existed. Lastly, the current study focused on the 1-year changes in RRF and echocardiographic parameters; therefore, the results might be different with an extended study period of 2 or 3 years.

Despite these limitations, we believe that the present study is a meaningful investigation demonstrating for the first time that cardiac performance is significantly worsened or less improved in incident PD patients with rapid RRF decline. In addition, rapid RRF decline rate is found to be a significant independent predictor of adverse clinical outcomes including CV composite, technique failure, and PD peritonitis. Based on these findings, preservation of RRF is important for conserving cardiac performance, resulting in an improvement in clinical outcome in incident PD patients.

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