ORIGINAL ARTICLE

Tissue Doppler imaging predicts outcomes in hemodialysis patients with preserved left ventricular function

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Abstract

Background: Cardiovascular disease is a major cause of mortality in patients with end-stage renal disease (ESRD). In addition to arteriosclerosis (arterial stiffness) and atherosclerosis, left ventricular (LV) hypertrophy and LV systolic dysfunction are the major cardiac determinants of cardiovascular mortality in hemodialysis patients. Although LV diastolic dysfunction is common in patients with ESRD, its prognostic value is yet to be established.

Methods: A total of 103 ESRD patients (52 females, 51 males, age 51 ± 14 years) receiving regular hemodialysis and with preserved LV systolic function were prospectively enrolled in the current study. A comprehensive cardiovascular evaluation was performed at baseline. LV diastolic function was assessed using Doppler mitral inflow velocity and tissue Doppler imaging (TDI) of the mitral annulus velocity. Predictors for hospitalization and all-cause mortality were identified via Cox proportional hazards analysis.

Results: There were 20 deaths and 46 hospitalizations during a follow-up period of 67.9 ± 20.2 months. After adjusting for age, aortic pulse wave velocity (PWV), and carotid intima media thickness, Cox analysis demonstrated that ratio of early ventricular filling velocity (E) to early diastolic tissue velocity mitral annulus (E') (E/E') was a significant predictor for hospitalization (hazard ratio [HR] 1.235 and 95% CI 1.115-1.368 per-1SD). E' also independently predicted mortality (HR 0.682, 95% CI 0.472-0.985). The TDI parameters significantly correlated with the LV mass index and PWV.

Conclusion: The findings of the current study suggest that diastolic function, as indexed by TDI, is an independent predictor of hospitalization and mortality in ESRD patients receiving regular hemodialysis and with preserved LV systolic function. The TDI parameters may reflect the impairment of arterial function and LV pressure overload.

Keywords: End stage renal disease; Mitral annular motion velocity

1. INTRODUCTION

Patients with end-stage renal disease (ESRD) have a high mortality rate, primarily due to cardiovascular causes.[1] Arterial factors including atherosclerosis and arteriosclerosis[2–5] and ventricular remodeling and performance, such us left ventricular (LV) systolic dysfunction[6] and LV hypertrophy (LVH), are all major determinants of mortality in ESRD patients.[7] There is high prevalence of LVH[8] and the association between diastolic dysfunction and LVH has been illustrated in patients with ESRD.[9] However, the prognostic significance of diastolic dysfunction in ESRD patients with preserved systolic function is not comprehensively understood.

Tissue Doppler imaging (TDI) is a technique used to assess myocardial motion, which is a sensitive index of ventricular relaxation; it is less dependent on the loading condition and is therefore a more reliable diastolic function index. At present, the early diastolic mitral inflow velocity to early diastolic mitral annulus velocity (E/E') ratio is used to evaluate LV filling pressure, and it has been used as a marker for the diagnosis of diastolic heart failure.[10,11]

In the current study, it was investigated whether the E/E' ratio and/or E' could predict the incidence of mortality and hospitalization in ESRD patients receiving regular hemodialysis and who had preserved LV systolic function.

2. METHODS

2.1. Subjects

A total of 126 patients were assessed for inclusion in the present study. Patients were eligible for inclusion if they had been on maintenance hemodialysis for at least 3 months on dry body weight, as determined by their physician. Subjects with systolic function impairment, which was defined as left ventricular ejection fraction (LVEF) <50%, were excluded from the study. A total of 103 hemodialysis patients (51 men, 52 women) with a mean age of 51 ± 14 years were consecutively enrolled in the study. Sixteen of the patients (8.7%) had diabetes. All subjects provided written informed consent prior to their inclusion in the study, which had been approved by the institutional review board at the Taipei Veterans General Hospital. All participants received a comprehensive cardiovascular examination and blood tests on a mid-week nondialysis day.

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2.2. Echocardiography and cardiac measurements

Two-dimensional echocardiography was performed according to the recommendations of the American Society of Echocardiography.[12] LVEF was measured using the two-dimensional guided M-mode method, and the left atrial (LA) volume was measured using the cylinder method with two orthogonal apical views.[12] The LV mass index was the LV mass divided by body surface area. The trans-mitral blood flow was measured using pulsed-wave Doppler in an apical four-chamber view. The rate of early diastolic blood flow (peak velocity of the mitral early filling, E), the rate of late diastolic blood flow (peak velocity of the mitral late filling, A), the ratio of E/A, and the deceleration time of the E wave were measured. The early mitral annular velocity (E') was measured by tissue Doppler at septal site and the E/E' ratio was calculated.

2.3. Arterial factors

Arterial structure and function were assessed using ultrasound (Philips SONOS 5500, Andover, MA, USA) and arterial tonometry. Supine brachial systolic blood pressure (SBP) and diastolic blood pressure (DBP) were calculated by taking the average of four measurements obtained using an oscillometric device. Pulse pressure (PP) was the difference between SBP and DBP. Mean blood pressure was DBP + 1/3 PP. The measured arterial structural parameter was carotid intima-media thickness (cIMT). The arterial functional parameters included aortic pulse wave velocity (PWV) and the carotid augmentation index, which were acquired as previously reported.[13]

2.4. Follow-up

The date and causes of death for the deceased patients were collected by both telephone contact and review of hospital charts and death certificates, which were coded according to the International Classification of Disease, Ninth Revision (ICD-9). The ICD-9 codes used for cardiovascular death were 390-459.

2.5. Statistical analysis

Normally distributed continuous variables were presented as the mean ± SD and categorical variables were expressed as absolute numbers and relative frequencies. Student's *t*-test or $\chi 2$ tests were used to analyze the baseline characteristics where appropriate. Cox proportional hazard models were used to evaluate the independence of the tissue Doppler index in the prediction of outcomes, with adjustments for confounders. The prognostic differences across the subgroups were analyzed using Kaplan–Meier survival analysis. All statistical analyses were performed using SPSS software version 17.0 (SPSS, Inc., Chicago, IL, USA). All tests performed were two-sided and a p-value < 0.05 was considered to indicate a statistically significant difference.

3. RESULTS

There were 20 deaths and 46 hospitalizations during a follow-up period of 67.9 ± 20.2 months. There were eight cardiovascular and 12 noncardiovascular deaths. Table 1 lists the baseline characteristics of the study population and a comparison of the death and survival groups. The average time after initiation of dialysis was 36.0 ± 24.2 months. The etiologies of ESRD included chronic glomerulonephritis (36.1%), chronic interstitial nephritis (10.4%), diabetes nephropathy (9.5%), and others (including lupus nephritis, hypertensive nephrosclerosis, and polycystic kidney disease; 20%). The remaining cases were of unknown etiology. The death group was characterized by older age, larger LA diameter, lower E', higher E/E' ratio, and increased PWV and cIMT, compared with the survival group (Table 1). Underlying

Table 1

Baseline characteristics of the study population

	All (n = 103)	Survival (n = 83)	Mortality (n = 20)	*p*
Age, y	50.8 ± 13.5	48.5 ± 13.1	60.0 ± 11.0	0.001
Gender (male/%)	51 (46.5)	43 (51.8)	8 (40.0)	0.34
Height, cm	160.4 ± 8.7	160.8 ± 8.7	158.7 ± 8.5	0.33
Weight, kg	57.6 ± 10.3	57.9 ± 10.9	56.4 ±7.2	0.57
Systolic BP, mmHg	127.4 ± 29.4	126.0 ± 30.8	133.2 ± 22.5	0.32
Diastolic BP, mmHg	70.9 ± 16.6	70.8 ± 18.1	71.3 ± 8.5	0.84
Comorbidity				
Hypertension, %	33 (33.6)	28 (35.4)	5 (26.3)	0.45
Diabetes mellitus, %	9 (9.1)	6 (7.6)	3 (15.8)	0.26
Cardiovascular disease, %	4 (4.0)	4 (5.1)	0 (0)	0.31
Echocardiography				
ºLAD, cm	3.4 ± 0.5	3.3 ± 0.5	3.6 ± 0.4	0.02
ºLVID diastole, cm	4.6 ± 0.6	4.6 ± 0.6	4.5 ± 0.7	0.40
ºLVID systole, cm	2.7 ± 0.5	2.8 ± 0.5	2.6 ± 0.5	0.36
ºLV mass index, g/m^2	116.3 ± 38.1	114.5 ± 35.9	123.8 ± 46.2	0.32
ºMV E inflow, cm/s	77.0 ± 20.4	75.7 ± 20.1	82.9 ± 21.3	0.18
ºMV A inflow, cm/s	88.1 ± 20.9	86.2 ± 20.6	96.3 ± 20.6	0.05
ºE/A ratio	0.9 ± 0.3	0.9 ± 0.3	0.9 ± 0.2	0.83
ºMV deceleration time, ms	208.2 ± 53.1	211.6 ± 53.9	192.4 ± 47.5	0.17
ºIVRT, ms	94.3 ± 23.8	95.6 ± 24.5	89.0 ± 20.6	0.26
ºE', cm/s	7.7 ± 1.9	8.0 ± 1.7	6.5 ± 2.2	0.005
ºE/E'	9.9 ± 3.0	9.6 ± 2.9	11.8 ± 3.0	0.011
ºLVEF, %	64.5 ± 5.2	64.6 ± 5.0	64.9 ± 5.9	0.70
PWV, cm/s	915.8 ± 326.6	880.8 ± 299.8	1061.2 ± 396.1	0.02
cIMT, μm	73.2 ± 11.9	72.0 ± 11.4	78.0 ± 13.3	0.04
Laboratory findings				
ºHematocrit, %	31.1 ± 9.5	31.9 ± 10.5	28.0 ± 3.7	0.11
ºCalcium, mg/dL	9.5 ± 4.1	9.6 ± 4.6	9.1 ± 1.2	0.61
ºPhosphate, mg/dL	5.6 ± 2.4	5.7 ± 2.6	5.2 ± 1.2	0.41
Kt/V	1.54 ± 0.28	1.54 ± 0.29	1.51 ± 0.23	0.70

BP = blood pressure; cIMT = carotid intima media thickness; E/A ratio = ratio of the early (E) to late (A) ventricular filling velocities; E/E' = ratio of early ventricular filling velocity (E) to early diastolic tissue velocity mitral annulus (E'); LA = left atrial; LV = left ventricular; LVEF = left ventricular ejection fraction; LVID = left ventricular internal dimension; MV = mitral valve; PWV = pulse wave velocity.

Table 2

Univariable Cox regression model to predict long-term mortality and hospitalization

	Mortality	Hospitalization
	Hazard ratio (95% CI)	Hazard ratio (95% CI)
Age, y	1.061 (1.026-1.096)	1.050 (1.028-1.073)
Diabetes mellitus, %	1.012 (0.362-2.825)	1.012 (0.362-2.825)
CVD, %	1.091 (0.264-4.505)	1.091 (0.264-4.505)
LA diameter, cm	2.305 (1.032-5.152)	1.837 (1.067-3.161)
E', cm/s	0.571 (0.413-0.791)	0.794 (0.682-0.926)
E/E'	1.171 (1.039-1.319)	1.126 (1.149-1.392)
PWV, cm/s	1.001 (1.000-1.002)	1.001 (1.000-1.004)
cIMT, μm	1.032 (0.999-1.067)	1.023 (1.001-1.047)

cIMT = carotid intima media thickness; CVD = cardiovascular disease; E' = early diastolic tissue velocity mitral annulus; E/E' = ratio of early ventricular filling velocity (E) to early diastolic tissue velocity mitral annulus; LA = left atrial; PWV = pulse wave velocity.

comorbidities, including hypertension, diabetes, and cardiovascular disease were similarly distributed across both groups.

3.1. Predictors of mortality and hospitalization

The risk factors associated with all-cause mortality and hospitalization are shown in Table 2. Age, cIMT, PWV, LA diameter, E', and E/E' were all significant predictors of all-cause death and/or hospitalization (Table 2). Underlying diseases, such as diabetes or cardiovascular diseases could predict neither morality nor hospitalization. A Kaplan–Meier curve showed that those with high LV end-diastolic pressure (E/E' ≥ 15) had an increased risk of hospitalization (Fig. 1). In multiple cox proportional hazard models, E' could predict mortality (hazard ratio [HR] 0.682 and 95% CI 0.472-0.985 per-1SD) after accounting for age, cIMT, and PWV (Table 3). The E/E' ratio was an independent predictor of the risk of hospitalization (HR 1.235 and 95% CI 1.115-1.368 per-1SD) (Table 3).

3.2. Determinants of E' and the E/E' ratio

To investigate any correlations between E' and the E/E' ratio, stepwise multiple linear regression analysis was performed using age, LV mass index, PWV, LA diameter, and the concentrations of serum calcium and phosphates. PWV, age, and LV mass index formed the maximum predictive model for E' and the attributable proportions of the total explained variance were 73.4%, 17.3%, and 9.5%, respectively (Fig. 2A). Regarding the E/E' ratio, it significantly correlated with LA diameter, age, and LV mass index, and the attributable proportions were 65.1%, 20.7%, and 14.1%, respectively (Fig. 2B).

Table 3

Multivariable Cox regression model to predict long-term mortality and hospitalization

	Mortality	Hospitalization
	Hazard ratio (95% CI)	Hazard ratio (95% CI)
LA diameter, cm	2.005 (0.913-4.402)	1.675 (0.988-2.842)
E', cm/s	0.682 (0.472-0.985)	0.902 (0.760-1.070)
E/E'	1.119 (0.982-1.275)	1.235 (1.115-1.368)

*Adjustment for age = carotid intima media thickness = and pulse wave velocity.
E' = early diastolic tissue velocity mitral annulus; E/E' = ratio of early ventricular filling velocity (E) to early diastolic tissue velocity mitral annulus; LA = left atrial.

4. DISCUSSION

In the present study, it was found that diastolic dysfunction, as evaluated by tissue Doppler, was an independent predictor of hospitalization and all-cause mortality in patients with ESRD receiving regular hemodialysis and with preserved LVEF. It was further illustrated that LA diameter, LV mass, arterial stiffness, and age were major determinants of diastolic dysfunction.

4.1. Arteriosclerosis, atherosclerosis, and LVH in ESRD patients

The mortality rate of ESRD patients remains high despite advances in dialysis facilities and techniques; cardiovascular disease is the leading cause of mortality in these patients. Previous studies have demonstrated that both arteriosclerosis and atherosclerosis are major determinants of outcomes in ESRD patients.[2–5] In addition to these arterial factors, LV systolic dysfunction and LVH are also associated with unfavorable outcome in ESRD patients.[6,7,14] There is a high prevalence of LVH[8] in patients with ESRD; however, the prevalence of LV systolic dysfunction is less frequent.[14,15] A significant portion of ESRD patients present with LVH and diastolic dysfunction,[9] and the prevalence of diastolic dysfunction increased as renal function deteriorated in patients with autosomal dominant polycystic kidney disease.[16]

4.2. TDI parameters as clinical risk factors in ESRD

Diastolic function has been shown to be a predictor of mortality and cardiovascular events in patients with chronic kidney disease.[9] Han et al[17] demonstrated that diastolic dysfunction is an independent predictor of cardiovascular outcomes in dialysis patients with preserved LV systolic function. These studies highlighted the importance of diastolic function in the evaluation and follow-up of ESRD patients; however, they did not consider arterial factors. There is complex ventricular-arterial coupling in

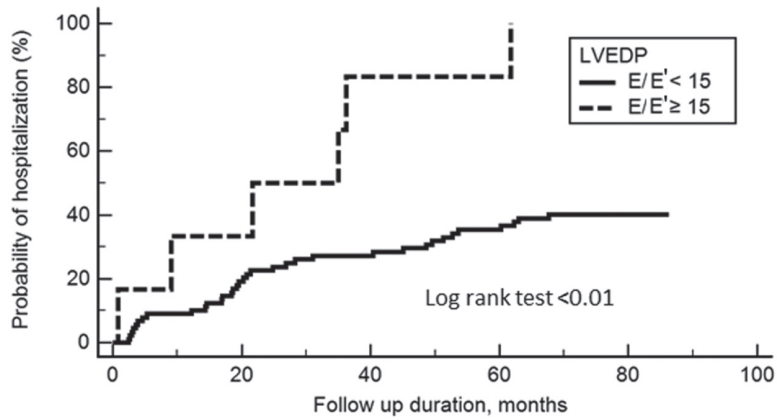

Fig. 1 Kaplan–Meier curve analysis for hospitalization of the study population, according to the ratio of early ventricular filling velocity to early diastolic tissue velocity mitral annulus (E/E'). E/E' ≥ 15 reflects a high LVEDP. E/E', ratio of early ventricular filling velocity to early diastolic tissue velocity mitral annulus; LVEDP, left ventricular end-diastolic pressure.

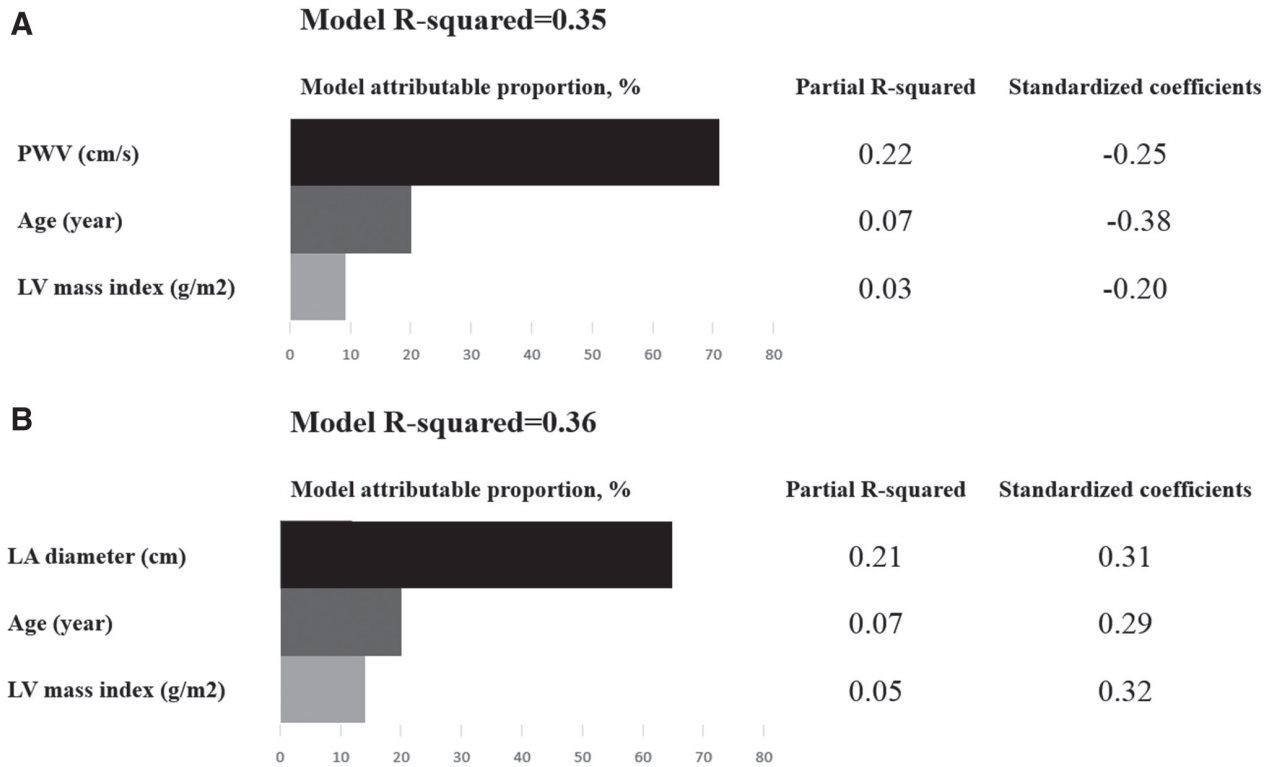

Fig. 2 The determinants of tissue Doppler imaging parameters, including (A) E' and (B) E/E', and their proportional contributions as calculated using multiple linear regression stepwise analyses. E', early diastolic tissue velocity mitral annulus; E/E', ratio of early ventricular filling velocity to early diastolic tissue velocity mitral annulus; LA, left atrial; LV mass index, left ventricular mass index; PWV, pulse wave velocity.

ESRD patients.[13] Previous studies have demonstrated that LVH and diastolic dysfunction are associated with vascular calcification and arterial stiffness.[18,19] The findings of the current study further support that the diastolic function index, as determined by TDI, can independently predict mortality and hospitalization after considering the important arterial factors.

To minimize the effect of volume status on the E/E' ratio, which was considered to be less preload dependent, an echography was performed after dry weight was achieved and on the next day after hemodialysis. After adjusting for confounding factors, E' and the E/E' ratio were still significant predictors of poor outcomes in ESRD patients undergoing hemodialysis. This finding is consistent with previous studies.[17,20,21] The E/E' ratio has been recommended as a noninvasive tool for estimating the LV filling pressure and is widely used in clinical echocardiography.[11] It should also be considered during the evaluation of cardiovascular status in ESRD patients.

4.3. Determinants of diastolic dysfunction in ESRD patients

Diastolic dysfunction has a complex presentation in patients with ESRD; it not only involves the myocardium but also age, plasma levels of calcium and phosphate, arterial calcification, aortic stiffness, and volume status.[22–24] The present study conducted a multiple linear regression stepwise analysis and revealed that the major determinants of TDI parameters included age, LA diameter, LV mass index and PWV. However, it should be noted that PWV, age and LV mass index explained 35% of the total variance of E'. LA diameter, age and LV mass index could explain 36% of the total variance of E/E' ratio. These findings further support the idea that diastolic dysfunction is a complex process in patients with ESRD, as not only cardiovascular function but other conditions related to ESRD are involved.[22–24] A previous study by the authors also demonstrated that the diastolic function parameters and arterial function are relatively volume dependent.[25,26] The effect of volume change was limited by collecting the data on a mid-week nondialysis day. The hematocrit and plasma level of calcium and phosphate during analysis were also considered. However, other ERSD-related factors might play a role but have not been included in the current analysis.

4.4. Study limitations

There were several limitations in the present study. First, there were only a small number of patients enrolled, so the specific causes of death could not be further analyzed. Second, diabetics comprised only 9% of the study population. This might be the reason for the relatively good prognosis in this population; however, it may limit the ability to generalize the findings to the whole ESRD population. Third, sequent follow-up echocardiography data was not available.

In conclusion, diastolic dysfunction, as indexed by TDI, is an independent predictor of mortality and hospitalization in ERSD patients receiving regular hemodialysis and with preserved LV systolic function. The TDI parameters reflected the impairment of arterial function and LV pressure overload with the resultant LV hypertrophy. E' and the E/E' ratio should be incorporated in the evaluation of the cardiovascular status of ESRD patients.

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REFERENCES

1. Patients E. Chapter 5: mortality. *Am J Kidney Dis* 2015;**66**:S145–52.
2. London GM, Blacher J, Pannier B, Guerin AP, Marchais SJ, Safar ME. Arterial wave reflections and survival in end-stage renal failure. *Hypertension* 2001;**38**:434–8.
3. Blacher J, Asmar R, Djane S, London GM, Safar ME. Aortic pulse wave velocity as a marker of cardiovascular risk in hypertensive patients. *Hypertension* 1999;**33**:1111–7.

4. Blacher J, Guerin AP, Pannier B, Marchais SJ, Safar ME, London GM. Impact of aortic stiffness on survival in end-stage renal disease. *Circulation* 1999;**99**:2434–9.
5. Benedetto FA, Mallamaci F, Tripepi G, Zoccali C. Prognostic value of ultrasonographic measurement of carotid intima media thickness in dialysis patients. *J Am Soc Nephrol* 2001;**12**:2458–64.
6. Yu WC, Lin YP, Chuang SY, Lin IF, Chen CH. Cardiovascular determinants of prognosis in normotensive hemodialysis patients. *BMC Nephrol* 2012;**13**:115.
7. Silberberg JS, Barre PE, Prichard SS, Sniderman AD. Impact of left ventricular hypertrophy on survival in end-stage renal disease. *Kidney Int* 1989;**36**:286–90.
8. Foley RN, Parfrey PS, Harnett JD, Kent GM, Martin CJ, Murray DC, et al. Clinical and echocardiographic disease in patients starting end-stage renal disease therapy. *Kidney Int* 1995;**47**:186–92.
9. Kim MK KB, Lee JY, Kim JS, Han BG, Choi SO, Yang JW. Tissue Doppler-derived E/E' ratio as a parameter for assessing diastolic heart failure and as a predictor of mortality in patients with chronic kidney disease. *Korean J Intern Med* 2012;**28**:35–44.
10. Hillis GS, Moller JE, Pellikka PA, Gersh BJ, Wright RS, Ommen SR, et al. Noninvasive estimation of left ventricular filling pressure by E/E' is a powerful predictor of survival after acute myocardial infarction. *J Am Coll Cardiol* 2004;**43**:360–7.
11. Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. *J Am Soc Echocardiogr* 2009;**22**:107–33.
12. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2015;**28**:1–39.e14.
13. Lin YP, Chen CH, Yu WC, Hsu TL, Ding PY, Yang WC. Left ventricular mass and hemodynamic overload in normotensive hemodialysis patients. *Kidney Int* 2002;**62**:1828–38.
14. Zoccali C, Benedetto FA, Mallamaci F, Tripepi G, Giacone G, Cataliotti A, et al. Prognostic value of echocardiographic indicators of left ventricular systolic function in asymptomatic dialysis patients. *J Am Soc Nephrol* 2004;**15**:1029–37.
15. Foley RN, Parfrey PS, Kent GM, Harnett JD, Murray DC, Barre PE. Serial change in echocardiographic parameters and cardiac failure in end-stage renal disease. *J Am Soc Nephrol* 2000;**11**:912–6.
16. de Almeida EA, de Oliveira EI, Lopes JA, Almeida AG, Lopes MG, Prata MM. Diastolic function in several stages of chronic kidney disease in patients with autosomal dominant polycystic kidney disease: a tissue Doppler imaging study. *Kidney Blood Press Res* 2007;**30**:234–9.
17. Han JH, Han JS, Kim EJ, Doh FM, Koo HM, Kim CH, et al. Diastolic dysfunction is an independent predictor of cardiovascular events in incident dialysis patients with preserved systolic function. *PloS one* 2015;**10**:e0118694.
18. Nitta K, Akiba T, Uchida K, Otsubo S, Otsubo Y, Takei T, et al. Left ventricular hypertrophy is associated with arterial stiffness and vascular calcification in hemodialysis patients. *Hypertens Res* 2004;**27**:47–52.
19. Yoon HE, Chung S, Whang HC, Shin YR, Hwang HS, Chung HW, et al. Abdominal aortic calcification is associated with diastolic dysfunction, mortality, and nonfatal cardiovascular events in maintenance hemodialysis patients. *J Korean Med Sci* 2012;**27**:870–5.
20. Kim MK, Kim B, Lee JY, Kim JS, Han BG, Choi SO, et al. Tissue Doppler-derived E/E' ratio as a parameter for assessing diastolic heart failure and as a predictor of mortality in patients with chronic kidney disease. *Korean J Intern Med* 2013;**28**:35–44.
21. Wang AY, Wang M, Lam CW, Chan IH, Zhang Y, Sanderson JE. Left ventricular filling pressure by Doppler echocardiography in patients with end-stage renal disease. *Hypertension* 2008;**52**:107–14.
22. Fijalkowski M, Koprowski A, Gruchala M, Galaska R, Debska-Slizien A, Rogowski J, et al. Effect of preload reduction by hemodialysis on myocardial ultrasonic characterization, left atrial volume, and Doppler tissue imaging in patients with end-stage renal disease. *J Am Soc Echocardiogr* 2006;**19**:1359–64.
23. Galetta F, Cupisti A, Franzoni F, Femia FR, Rossi M, Barsotti G, et al. Left ventricular function and calcium phosphate plasma levels in uraemic patients. *J Intern Med* 2005;**258**:378–84.
24. Freitas VC, Danzmann LC, Torres MR. Left ventricular diastolic function in hemodialysis patients: role of preload increase maneuver on tissue Doppler imaging evaluation. *Am J Nephrol* 2006;**26**:469–75.
25. Lin YP, Yu WC, Hsu TL, Ding PY, Yang WC, Chen CH. The extracellular fluid-to-intracellular fluid volume ratio is associated with large-artery structure and function in hemodialysis patients. *Am J Kidney Dis* 2003;**42**:990–9.
26. Yu WC, Lee WS, Huang WP, Wu CC, Lin YP, Chen CH. Evaluation of cardiac function by tissue Doppler echocardiography: hemodynamic determinants and clinical application. *Ultrasound Med Biol* 2005;**31**:23–30.