RESEARCH ARTICLE

Association of the Ratio of Early Mitral Inflow Velocity to the Global Diastolic Strain Rate with a Rapid Renal Function Decline in Atrial Fibrillation

Szu-Chia Chen1,3,4,5, Wen-Hsien Lee2,3,4, Po-Chao Hsu2,4, Chee-Siong Lee2,4, Meng-Kuang Lee2,3, Hsueh-Wei Yen2,4, Tsung-Hsien Lin2,4, Wen-Chol Voon2,4, Wen-Ter Lai2,4, Sheng-Hsiung Sheu2,4, Ho-Ming Su2,3,4*

1 Division of Nephrology, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, 2 Division of Cardiology, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, 3 Department of Internal Medicine, Kaohsiung Municipal Hsiao-Kang Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan, 4 Faculty of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan, 5 Graduate Institute of Clinical Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

* cobeshm@seed.net.tw

Abstract

The ratio of early mitral inflow velocity (E) to the global diastolic strain rate (E’sr) has been correlated with left ventricular filling pressure and predicts adverse cardiac outcomes in atrial fibrillation (AF). The relationship between the E/E’sr ratio and renal outcomes in AF has not been evaluated. This study examined the ability of the E/E’sr ratio in predicting progression to the renal endpoint, which is defined as a ≥ 25% decline in the estimated glomerular filtration rate in patients with AF. Comprehensive echocardiography was performed on 149 patients with persistent AF, and E’sr was assessed from three standard apical views using the index beat method. During a median follow-up period of 2.3 years, 63 patients (42.3%) were reaching the renal endpoint. Multivariate analysis showed that an increased E/E’sr ratio (per 10 cm) (hazard ratio, 1.230; 95% confidence interval, 1.088 to 1.391; p = 0.001) was associated with an increased renal endpoint. In a direct comparison, the E/E’sr ratio outperformed the ratio of E to early diastolic mitral annular velocity (E’/E) in predicting progression to the renal endpoint in both univariate and multivariate models (p = 0.039). Moreover, adding the E/E’sr ratio to a clinical model and echocardiographic parameters provided an additional benefit in the prediction of progression to the renal endpoint (p = 0.006). The E/E’sr ratio is a useful parameter and is stronger than the E/E’ ratio in predicting the progression to the renal endpoint, and it may offer an additional prognostic benefit over conventional clinical and echocardiographic parameters in patients with AF.
Introduction

Atrial fibrillation (AF) is the most common form of cardiac arrhythmia and its prevalence increases with age, reaching a prevalence rate of 8% in individuals older than 80 years [1, 2]. Furthermore, AF is associated with an increased risk of stroke, heart failure, and all-cause mortality [3]. Recently, we found that anemia and echocardiographic systolic and diastolic parameters from traditional echocardiography are useful predictors of cardiovascular outcomes in patients with AF [4]. In patients with AF, a relative reduction (≥ 25%) in the estimated glomerular filtration rate (eGFR) independently predicts the risk of stroke and death [5]. Therefore, identifying AF patients with rapid renal function progression for aggressive treatment interventions is crucial in disease attenuation and prolonged survival.

Echocardiographic measures of left ventricular (LV) function and structure have been reported to predict adverse renal outcomes in advanced chronic kidney disease (CKD) patients from 2-D and tissue Doppler echocardiography [6, 7]. We have reported that impaired LV systolic and diastolic functions were associated with a rapid renal function decline and progression to dialysis in patients without AF [7, 8]. The LV early global diastolic strain rate (E\text{'sr}) was reported to be a useful parameter of an LV diastolic function [9]. Furthermore, several studies have demonstrated a close correlation between invasively measured LV filling pressure and the ratio of early mitral inflow velocity (E) to E\text{'sr} [10–12]. Recently, we reported that the E/E\text{'sr} ratio was associated with adverse cardiac events in patients with AF [13]. However, its relationship with renal outcomes in patients with AF has not been evaluated. Accordingly, this study assessed whether the E/E\text{'sr} ratio is a useful parameter in the prediction of progression to the renal endpoint (a ≥ 25% decline in eGFR) in patients with AF.

Methods

Study participants

This observational cohort study prospectively and consecutively included patients with persistent AF referred for echocardiographic examinations to Kaohsiung Municipal Hsiao-Kang Hospital from April 2010 to July 2012. Persistent AF is defined as AF lasting 7 days, which is confirmed using 12-lead electrocardiography, 24-hour Holter electrocardiography, or electrocardiographic recording during echocardiographic examination. Patients with moderate and severe mitral stenosis, moderate and severe aortic stenosis or regurgitation, severe mitral regurgitation, or inadequate echocardiographic visualization were excluded. In addition, patients with fewer than three eGFR measurements during the follow-up period and patients without a follow-up of more than 6 months after enrollment were also excluded to avoid incomplete observation of changes in the renal function. Finally, 149 patients (mean age 69.8 ± 9.9 years, 104 male) were included in this study.

Ethics statement

The study protocol was approved by the Institutional Review Board of Kaohsiung Medical University Hospital (KMUH-IRB-20130062). Written informed consent was obtained from the patients, and all clinical investigations were conducted according to the principles expressed in the Declaration of Helsinki. The patients also consented to the publication of the clinical details.

Echocardiographic evaluation

An experienced cardiologist performed echocardiographic examination on participants respiring quietly in the left decubitus position by using Vivid 7 (GE Vingmed Ultrasound AS, Horten, Norway). The cardiologist was blinded to the clinical data, such as history of hypertension,
Two-dimensional and anatomic M-mode images were recorded from the standardized views. The Doppler sample volume was placed at the tips of the mitral leaflets to obtain the LV inflow waveforms from the apical four-chamber view. Pulsed Doppler tissue imaging was performed with the sample volume placed at the lateral and septal corners of the mitral annulus to obtain waveforms from the apical four-chamber view. Early diastolic mitral annular velocity (E') was averaged from measurements at septal and lateral annuli. The wall filter settings were adjusted to exclude high-frequency signals and the gain was minimized. The LV ejection fraction (LVEF) was measured using the modified Simpson's method, the LV mass was calculated using the modified Devereux method [14], the LV mass index (LVMI) was calculated by dividing the LV mass by the body surface area, the left atrial volume was measured using the biplane area-length method [15], and the left atrial volume index (LAVI) was calculated by dividing the left atrial volume by the body surface area.

LV apical four-chamber, two-chamber, and long-axis views were acquired using a high frame rate (50–90 frames/s). The endocardial border was manually defined using a point-and-click technique. An epicardial surface tracing was automatically generated by the system, creating a region of interest, which was manually adjusted to cover the full thickness of the myocardium in the systolic frame. The ventricular chamber was divided into six segments, and six segmental strain and strain rate curves were analyzed in each apical view. Peak segmental longitudinal systolic strain and early diastolic strain rate measurements were determined from these curves. E' was assessed in the 18 LV segments from the three standard apical views. The values in the 18 LV segments were averaged to obtain the mean value for later analysis. The minimum number of LV segments for acceptable E' measurements was 15. We used cine loops to determine the beat to be calculated. The raw ultrasonic data, including 15 consecutive beats from the three standard apical views, were recorded and analyzed offline by using EchoPAC version 08 (GE Vingmed Ultrasound AS).

The index beat was used to measure LV dimensions, the LVEF, LAVI, LVMI, and E' [9, 16, 17]. Because their measurements were easy and rapid, E, E-wave deceleration time (EDT), and E' were obtained from five beats [18] and then averaged for later analysis. If the cardiac cycle length was too short to complete the diastolic process, this beat was skipped. Thus, the selection of E, EDT, and E' was not always consecutive. In addition, the heart rate was determined from five consecutive beats.

Collection of demographic, medical, and laboratory data

Demographic and medical data including age, sex, and comorbid conditions were obtained from medical records and interviews with patients. The body mass index (BMI) was calculated as the ratio of weight in kilograms divided by the square of height in meters. Laboratory data were measured from fasting blood samples using an autoanalyzer (Roche Diagnostics GmbH, D-68298 Mannheim COBAS Integra 400). Serum creatinine was measured using the compensated Jaffé (kinetic alkaline picrate) method in a Roche/Integra 400 Analyzer (Roche Diagnostics, Mannheim, Germany) using a calibrator traceable to isotope-dilution mass spectrometry [19]. The value of eGFR was calculated using the four-variable equation in the Modification of Diet in Renal Disease (MDRD) study [20]. Dipsticks (Hema-Combistix, Bayer Diagnostics) were used to examine proteinuria. A test result of 1+ or more was defined as positive. Blood and urine samples were obtained within 1 month of enrollment. In addition, information regarding antihypertensive and other medications used by the patients during the study period, including angiotensin converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARB), β-blockers, calcium channel blockers, diuretics, and antiplatelet and anticoagulant drugs, was obtained from the medical records.
Definition of the renal endpoint

The renal endpoint was defined as a $\geq 25\%$ decline in eGFR since the enrollment of the patients [21]. For patients who were reaching the renal endpoint, the renal function data were censored. The patients who did not reach renal endpoints were followed up until the last serum creatinine measurement.

Statistical analysis

Statistical analysis was performed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA) for Windows. Data are expressed as percentages, mean ± standard deviation, or median (25th–75th percentile) for triglyceride and several serum creatinine measurements. The differences between groups were checked using a chi-squared test for categorical variables and independent t-test for continuous variables. The study participants were stratified into three groups according to tertiles of the E/E’s ratio. Tertile 1 was considered reference category. Multiple comparisons among the study groups were performed using one-way analysis of variance (ANOVA), followed by a post hoc test adjusted with a Bonferroni correction. Cox proportional hazards analyses were performed to investigate the associations of E/E’s ratio tertiles and the E/E’s ratio (continuous data) with progression to the renal endpoint. The adjusted covariates included age, sex, diabetes mellitus, hypertension, coronary artery disease, systolic and diastolic blood pressures, the BMI, fasting glucose, log triglyceride, total cholesterol, hemoglobin, baseline eGFR, uric acid, proteinuria, antihypertensive drug use, antiplatelet agents, anticoagulants, the LAVI, LVMI, LVEF, and EDT. Survival curve for the renal endpoint was derived using Kaplan–Meier analysis. A direct comparison between the E/E’s and E/E’s ratio was performed in both univariate and multivariate models. Incremental model performance was assessed using a change in the $\chi^2$ value. A difference was considered significant at $P < 0.05$.

Results

One hundred and forty-nine patients were included in this study. The mean age of the patients was 69.8 ± 9.9 years; 104 patients were male and 45 were female. During the follow-up period, the average number of serum creatinine measurements was nine (25th–75th percentile: 6–15). The E/E’s ratio was 63.0 ± 21.8 cm. The comparison of baseline characteristics and echocardiographic parameters between patients reaching and not reaching the renal endpoint is shown in Table 1. Sixty-three patients (42.3%) reached the renal endpoint. Compared with patients without renal endpoint, patients with a renal endpoint were observed to be older and had higher uric acid, LVMI, EDT, and E/E’s ratio, and lower LVEF and E’s.

The study participants were stratified into three groups according to tertiles of the E/E’s ratio ($< 51.9$, $\geq 51.9$ to $< 66.2$, and $\geq 66.2$ cm). A comparison of the clinical characteristics and echocardiographic parameters among the study groups is shown in Table 2. The three groups had 49, 50, and 50 patients. Significant differences in LVMI, LVEF, E, E’, E/E’s ratio, E’s, and E/E’s ratio were observed among patients in the different tertiles.

Risk of progression to the renal endpoint

The mean follow-up period was 2.3 ± 1.2 years. During the follow-up period, 63 patients (42.3%) reached the renal endpoint. Table 3 lists the hazard ratios (HRs) of the E/E’s ratio tertiles and E/E’s ratio for the renal endpoint with and without adjustment of the demographic, clinical, and biochemical factors. Patients with tertile 3 of the E/E’s ratio (versus tertile 1) were associated with an increased renal endpoint in an unadjusted model (HR, 2.161; 95% confidence interval [CI], 1.197 to 3.900; $p = 0.011$) and adjusted model (HR, 6.148; 95% CI, 1.990 to
Fig 1 illustrates the Kaplan–Meier curves for renal endpoint-free survival (log-rank \(p = 0.008\)) in all patients subdivided according to tertiles of the E/E’sr ratio. A similar pattern of association was observed using the E/E’sr ratio as a continuous variable. An increased E/E’sr ratio was associated with an increased renal endpoint in an unadjusted model (HR, 1.190; 95% CI, 1.087 to 1.302; \(p < 0.001\)) and an adjusted model (HR, 1.230; 95% CI, 1.088 to 1.391; \(p = 0.001\)).
The use of ACEIs or ARBs was not significantly associated with an increased renal endpoint in univariate analysis (HR, 1.338; 95% CI, 0.785 to 2.280; p = 0.284).

Comparison of the E/E’ and E/E’sr ratios in progression to the renal endpoint

In the univariate analysis, the E/E’sr ratio was significantly related to the renal endpoint and outperformed the E/E’ ratio of the model in a direct comparison ($\chi^2 = 14.24$ vs. 6.113,
In the multivariate analysis, an increased E/E′sr ratio was independently associated with an increased renal endpoint. In a direct comparison, the multivariate model without E/E′ and E/E′sr ratios (global $\chi^2 = 46.91$) was not significantly improved by adding the E/E′ ratio.
(global $\chi^2 = 47.29, p = 0.538$), whereas adding the E/E$'\text{sr}$ ratio resulted in significant improvement (global $\chi^2 = 51.15, p = 0.039$).

### Incremental value of the E/E$'\text{sr}$ ratio in relation to the renal endpoint

The incremental value of the E/E$'\text{sr}$ ratio in the outcome prediction is shown in Fig 2. The clinical model includes age, sex, diabetes mellitus, hypertension, coronary artery disease, systolic and diastolic blood pressures, the BMI, fasting glucose, log triglyceride, total cholesterol, hemoglobin, baseline eGFR, uric acid, proteinuria, antihypertensive drug use, antiplatelet agents, and anticoagulants ($\chi^2 = 30.77$). Adding the LAVI, LVMI, LVEF, EDT, and E/E$'$ ratio to the clinical model offered an additional benefit in the prediction of progression to the renal endpoint ($p = 0.008$). In addition, adding the E/E$'\text{sr}$ ratio to the model consisting of the clinical model, LAVI, LVMI, LVEF, EDT, and E/E$'$ ratio resulted in further significant improvement in the prediction of the renal endpoint ($p = 0.006$).

### Discussion

In this study, we evaluated the association of the E/E$'\text{sr}$ ratio with the progression to the renal endpoint in patients with AF. We observed that the increased E/E$'\text{sr}$ ratio was independently associated with an increase in the renal endpoint in patients with AF. In a direct comparison, the E/E$'\text{sr}$ ratio outperformed the E/E$'\text{sr}$ ratio in predicting progression to the renal endpoint in both univariate and multivariate models. Furthermore, the E/E$'\text{sr}$ ratio could add a significant incremental prognostic value beyond the conventional clinical and echocardiographic parameters.
The first major finding of our study was the identification of the E/E’sr ratio as a risk factor for progression to the renal endpoint in patients with AF. Recent studies have demonstrated that CKD patients with an increased LV filling pressure indicated by an increased LAVI, left atrial diameter, and E/E’ ratio from tissue Doppler echocardiography might have adverse renal outcomes [6, 22, 23]. In a recent study, we evaluated the association between the E/E’ and renal dysfunction progression, and observed that patients with a rapid renal function decline had a higher E/E’ [8]. Furthermore, a high E/E’ was independently associated with increased risk of commencement of dialysis in CKD patients [6]. In addition, our study revealed that increased E/E’sr was associated with an increase in the renal endpoint in patients with AF. Kusunose et al. [9] have demonstrated that the E’sr measured using the index beat in patients with AF is an accurate estimate of the E’sr measured from averaging multiple cardiac cycles and is significantly correlated with a time constant of isovolumic left ventricular pressure decay. In addition, they observed that E/E’sr was highly associated with LV filling pressure in patients with AF. This implied that AF patients with a high E/E’sr ratio might have a high volume status, thereby increasing renal efferent pressure and decreasing renal blood flow and finally causing a progressive renal function decline [24]. The higher preload status might contribute to a more rapid renal progression. Hence, an assessment of the E/E’sr ratio in patients with AF may facilitate identifying the high-risk group with adverse renal outcomes.

The second major finding of our study was that the E/E’sr ratio was a useful predictor and was stronger than the E/E’ ratio in predicting progression to the renal endpoint in patients with AF. Recently, we reported that the E/E’sr ratio is a useful parameter and is stronger than the E/E’ ratio in predicting adverse cardiac events in patients with AF [13]. E’ was developed to assess regional diastolic function, and its value for estimating a global diastolic function with regional functional abnormalities is limited [25]. In addition, the inherent limitations of Doppler-based methods, such as angle dependency with the potential for significant errors with angulations > 20°, may also preclude E’ from reflecting a truly early diastolic function. By contrast, E’sr derived from two-dimensional speckle-tracking echocardiography was recently introduced as a novel parameter to reflect LV relaxation function in patients with AF [9]. This imaging method discriminates between the active and passive myocardial motion and enables the angle-independent quantification of myocardial deformation in two dimensions. Hence, E’sr should be able to reflect the LV diastolic function more globally and accurately than E’ can.

The third major finding of this study was that adding the E/E’sr ratio to the model consisting of clinical parameters, the LAVI, LVEF, LVMI, EDT, and E/E’ ratio provided an additional benefit in the prediction of poor renal prognosis. Our previous data showed that concentric LVH was associated with progression to dialysis, and that an increased LA diameter and a decreased LVEF and midwall fractional shortening were associated with a rapid renal function decline [7]. In addition, Furukawa et al. [23] evaluated the LAVI factor in progression to hemodialysis in 140 patients with CKD stage 4–5. They observed that the LAVI was a risk factor for the period before dialysis. In our study, although conventional clinical and echocardiographic systolic and diastolic parameters were known, considering the E/E’sr ratio facilitated improving the renal outcome prediction in patients with AF. The E/E’sr ratio should be measured during echocardiographic examination for additional prognostication in these patients.

There were several limitations to this study. Because their measurement using the averaging method is time consuming, many echocardiographic parameters, including the LV dimensions, LVEF, LAVI, LVMI, and E’sr, were not obtained by averaging multiple cardiac cycles but were measured according to the index beat. However, several studies have proved that using the index beat to measure certain echocardiographic parameters, including LV systolic and diastolic functions and left atrial parameters, in patients with AF is as accurate as the time-
Two-dimensional speckle-tracking echocardiography generated longitudinal, radial, and circumferential deformation measurements and LV twist. In this study, only E’s was measured and analyzed. The majority of our patients were receiving long-term treatment involving antihypertensive, antiplatelet, and anticoagulant medications. For ethical reasons, we did not withdraw these medications. Hence, we could not exclude the influence of these medications on the present findings. However, we adjusted for the use of these medicines in the multivariate analysis. Because the subjects of this study were already being evaluated for heart disease by echocardiography, it was susceptible to selection bias, making our findings potentially less generalized.

In conclusion, our results demonstrated that the E/E’ ratio is a useful parameter and is stronger than the E/E’ ratio in predicting adverse renal outcomes in patients with AF, and it may offer an additional prognostic benefit over conventional clinical and echocardiographic parameters.

Supporting Information
S1 File. Relevant data including E/E’ sr and renal outcome.
(XLS)

Author Contributions
Conceived and designed the experiments: SCC WHL HMS. Performed the experiments: SCC WHL HMS. Analyzed the data: SCC WHL PCH HMS. Contributed reagents/materials/analysis tools: SCC WHL PCH CSL MKL HWY THL HMS WCV WTL SHS. Wrote the paper: SCC HMS.

References
1. Feinberg WM, Cornell ES, Nightingale SD, Pearce LA, Tracy RP, Hart RG, et al. Relationship between prothrombin activation fragment f1.2 and international normalized ratio in patients with atrial fibrillation. Stroke prevention in atrial fibrillation investigators. Stroke 1997; 28:1101–1106. PMID: 9183333

2. Go AS, Hylek EM, Phillips KA, Chang Y, Henault LE, Selby JV, et al. Prevalence of diagnosed atrial fibrillation in adults: National implications for rhythm management and stroke prevention: The anticoagulation and risk factors in atrial fibrillation (atria) study. JAMA 2001; 285:2370–2375. PMID: 11343485

3. Fuster V, Ryden LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation—executive summary: A report of the american college of cardiology/american heart association task force on practice guidelines and the european society of cardiology committee for practice guidelines (writing committee to revise the 2001 guidelines for the management of patients with atrial fibrillation). J Am Coll Cardiol 2006; 48:854–906. PMID: 16904574

4. Lee WH, Hsu PC, Chu CY, Lee HH, Lee MK, Lee CS, et al. Anemia as an Independent Predictor of Adverse Cardiac Outcomes in Patients with Atrial Fibrillation. Int J Med Sci 2015; 12:618–624. doi: 10.7150/ijms.11924 PMID: 26283880

5. Guo Y, Wang H, Zhao X, Zhang Y, Zhang D, Ma J, et al. Sequential changes in renal function and the risk of stroke and death in patients with atrial fibrillation. Int J Cardiol 2013; 168:4678–4684. doi: 10.1016/j.ijcard.2013.07.179 PMID: 23972369

6. Chen SC, Chang JM, Tsai YC, Huang JC, Chen Li, Su HM, et al. Ratio of transmitral e-wave velocity to early diastole mitral annulus velocity with cardiovascular and renal outcomes in chronic kidney disease. Nephron Clin Pract 2013; 123:52–60. doi: 10.1159/000351513 PMID: 23774331

7. Chen SC, Su HM, Hung CC, Chang JM, Liu WC, Tsai JC et al. Echocardiographic parameters are independently associated with rate of renal function decline and progression to dialysis in patients with chronic kidney disease. Clin J Am Soc Nephrol 2011; 6:2750–2758. doi: 10.2215/CJN.04660511 PMID: 21980185

8. Chen SC, Lin TH, Hsu PC, Chang JM, Lee CS, Tsai WC, et al. Impaired left ventricular systolic function and increased brachial-ankle pulse-wave velocity are independently associated with rapid renal function progression. Hypertens Res 2011; 34:1052–1058. doi: 10.1038/hr.2011.95 PMID: 21753773
9. Kusunose K, Yamada H, Nishio S, Tomita N, Hotchi J, Bando M, et al. Index-beat assessment of left ventricular systolic and diastolic function during atrial fibrillation using myocardial strain and strain rate. J Am Soc Echocardiogr 2012; 25:953–959. doi: 10.1016/j.echo.2012.06.009 PMID: 22763085

10. Dokainish H, Sengupta R, Pillai M, Bobek J, Lakkis N. Usefulness of new diastolic strain and strain rate indexes for the estimation of left ventricular filling pressure. Am J Cardiol 2008; 101:1504–1509. doi: 10.1016/j.amjcard.2008.01.037 PMID: 18471466

11. Kimura K, Takenaka K, Ebihara A, Okano T, Uno K, Fukuda N, et al. Speckle tracking global strain E/E' predicts lv filling pressure more accurately than traditional tissue doppler E/E'. Echocardiography 2012; 29:404–410. doi: 10.1111/j.1540-8175.2011.01587.x PMID: 22066607

12. Wang J, Khoury DS, Thohan V, Torre-Amione G, Naguet SF. Global diastolic strain rate for the assessment of left ventricular relaxation and filling pressures. Circulation 2007; 115:1376–1383. PMID: 17339549

13. Hsu PC, Lee WH, Chu CY, Lee CS, Yen HW, Su HM, et al. The ratio of early mitral inflow velocity to global diastolic strain rate as a useful predictor of cardiac outcomes in patients with atrial fibrillation. J Am Soc Echocardiogr 2011; 24:1141–1147. doi: 10.1016/j.echo.2011.07.002 PMID: 21865011

14. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. Recommendations for chamber quantification: A report from the american society of echocardiography's guidelines and standards committee and the chamber quantification writing group, developed in conjunction with the european association of echocardiography, branch of the european society of cardiology. J Am Soc Echocardiogr 2005; 18:1440–1463. PMID: 16376782

15. Govindan M, Kiotsukoglu A, Saha SK, Borgulya G, Bajpai A, Bijnens BH, et al. Validation of echocardiographic left atrial parameters in atrial fibrillation using the index beat of preceding cardiac cycles of equal duration. J Am Soc Echocardiogr 2011; 24:1411–1417. doi: 10.1016/j.echo.2011.07.002 PMID: 21865011

16. Lee CS, Lin TH, Hsu PC, Chu CY, Lee WH, Su HM, et al. Measuring left ventricular peak longitudinal systolic strain from a single beat in atrial fibrillation: Validation of the index beat method. J Am Soc Echocardiogr 2012; 25:945–952. doi: 10.1016/j.echo.2012.06.006 PMID: 22763084

17. Sohn DW, Song JM, Zo JH, Chai IH, Kim HS, Chun HG, et al. Mitral annulus velocity in the evaluation of left ventricular diastolic function in atrial fibrillation. J Am Soc Echocardiogr 1999; 12:927–931. PMID: 10552353

18. Vickery S, Stevens PE, Dalton RN, van Lente F, Lamb EJ. Does the id-ms traceable mdrd equation work and is it suitable for use with compensated jaffe and enzymatic creatinine assays? Nephrol Dial Transplant 2006; 21:2439–2445. PMID: 16720592

19. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: A new prediction equation. Modification of diet in renal disease study group. Ann Intern Med 1999; 130:461–470. PMID: 10075613

20. Ford ML, Tomlinson LA, Chapman TP, Rajkumar C, Holt SG. Aortic stiffness is independently associated with rate of renal function decline in chronic kidney disease stages 3 and 4. Hypertension 2010; 55:1110–1115. doi: 10.1161/HYPERTENSIONAHA.109.143024 PMID: 20212289

21. Chen SC, Chang JM, Liu WC, Huang JC, Tsai JC, Lin MY, et al. Echocardiographic parameters are independently associated with increased cardiovascular events in patients with chronic kidney disease. Nephrol Dial Transplant 2012; 27:1064–1070. doi: 10.1093/ndt/gfr407 PMID: 21813825

22. Furukawa M, Ito H, Tanimoto M, Hagiwara S, Horikoshi S, Tomino Y. Predictive factors associated with the period of time before initiation of hemodialysis in ckd stages 4 and 5. Nephron Clin Pract 2011; 117:c341–347. doi: 10.1159/000321512 PMID: 20948232

23. Bock JS, Gottlieb SS. Cardiorenal syndrome: New perspectives. Circulation 2010; 121:2592–2600. doi: 10.1161/CIRCULATIONAHA.109.886473 PMID: 20547933

24. Hsiao SH, Chiou KR, Lin KL, Lin SK, Huang WC, Kuo FY, et al. Left atrial distensibility and e/e' for estimating left ventricular filling pressure in patients with stable angina. a comparative echocardiography and catheterization study. Circ J 2011; 75:1942–1950. PMID: 21646725