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Original Paper

Echocardiographic Changes in Patients with Stage 3–5 Chronic Kidney Disease and Left Ventricular Diastolic Dysfunction

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Key Words
Diastolic dysfunction · Chronic kidney disease · Tissue Doppler echocardiography

Abstract
Background: Left ventricular (LV) diastolic dysfunction in chronic kidney disease (CKD) patients frequently leads to the development of congestive heart failure. We evaluated changes in echocardiographic parameters among CKD patients with LV diastolic dysfunction. ***Methods:*** We examined 70 ambulatory patients with CKD at stages 3–5 and 26 patients without CKD as a control group. Standard echocardiography and tissue Doppler imaging were performed on all patients. Patients with CKD were divided into two groups according to the results of lateral mitral early diastolic velocity ($EmLV_{lat}$): a group with diastolic dysfunction (DD group; $EmLV_{lat}$ <8 cm/s) and a group without diastolic dysfunction (WDD group; $EmLV_{lat}$ ≥8 cm/s). ***Results:*** Compared to the patients in the WDD group, those in the DD group were characterized by lower values of mitral annular plane systolic excursion [MAPSE; 13 (11–17) vs. 14 (11–16) mm, $p < 0.0001$] and lateral mitral annular systolic velocity [$SmLV_{lat}$; 7 (5–14) vs. 8 (5–13) cm/s, $p = 0.006$]. The area under the receiver operating characteristic (ROC) curve of the MAPSE level for the detection of LV diastolic dysfunction was 0.801 [95% CI 0.684–0.890, $p < 0.0001$], whereas a ROC-derived MAPSE value of ≤13 mm was characterized by a sensitivity of 84.4% and a specificity of 75.8% for diagnosing LV diastolic dysfunction. The only independent variable predicting LV diastolic dysfunction was MAPSE [OR = 0.39; 95% CI 0.21–0.74, $p = 0.003$]. ***Conclusion:*** We showed that reduced MAPSE, but not $SmLV_{lat}$, is an independent predictive factor for LV diastolic dysfunction in CKD patients.

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Introduction

Myocardial dysfunction is common in patients with chronic kidney disease (CKD) – especially in the end stage of renal failure – and in dialysis patients. In CKD patients, left ventricular (LV) hypertrophy due to arterial hypertension and chronic anemia is one of the main reasons for developing congestive heart failure [1–4]. It is especially important to consider heart failure with preserved LV systolic function, which dominates in this population of patients. Echocardiography as a routine noninvasive imaging method is useful in determining diastolic dysfunction. In many previous studies, the significance of diastolic mitral annular velocities has been proven both in the analysis of diastolic dysfunction and as prognosis for CKD patients [5, 6]. In our study, we evaluated changes in echocardiographic parameters among CKD patients with LV diastolic dysfunction.

Methods

The study group consisted of 70 ambulatory patients with CKD at stages 3–5 with preserved LV systolic function defined by an LV ejection fraction (LVEF) >50%. Twenty-six patients without CKD were investigated as a control group. The exclusion criteria comprised the following: nonsinus rhythm, LV systolic dysfunction, previous myocardial infarction, cardiomyopathy, significant valvular heart disease and pericardial fluid >10 mm at diastole. Dialysis patients were excluded from our study.

The authors declare that they have complied with the Principles of Ethical Publishing presented in the Declaration of Helsinki and that the study protocol was approved by a local ethics committee.

Blood Pressure

Blood pressure was measured after resting in the supine position for 5 min and immediately before the echocardiographic examination by the same observer using a standard sphygmomanometer.

Echocardiography

Standard echocardiography was performed for all patients, using a GE 6S device with a 2.5- to 3.5-MHz transducer. Using the M-MODE in the parasternal long-axis view, the following parameters were assessed: LV end-diastolic dimension (LVEDD), right ventricular (RV) end-diastolic dimension (RVEDD), left atrial diastolic dimension (LAD), interventricular septal diastolic diameter (IVSDd) and LV posterior wall dimension at diastole (LVPWd). Additionally, LV fractional shortening (LVFS) was assessed. In a 4-chamber view, the LVEF was calculated by the modified Simpson's rule [7]. LV mass (LVM) was calculated with the formula recommended by the American Society of Echocardiography (ASE) modified by Devereux et al. [8]. The results obtained for the LVM were indexed to height in meters raised to the power of 2.7 ($LVM/Ht^{2.7}$) of the patient and presented as the LV mass index (LVMI) [7]. Using the M-MODE in a 4-chamber view, tricuspid and mitral annular plane systolic excursion (TAPSE and MAPSE) were assessed [9, 10].

In order to assess transmitral flow, pulsed-wave Doppler echocardiography was performed in a 4-chamber view. The Doppler gate was placed at the tips of the mitral valve leaflets, and a 2-phase flow profile was obtained, including early (E) and late (A) transmitral velocities and the deceleration time (DT) of the E wave; the E/A ratio was also calculated [7].

Tissue Doppler Echocardiography

In pulsed-wave tissue Doppler echocardiography, systolic and diastolic velocities were measured by placing the Doppler gate on the lateral mitral annulus at the posterior leaflet of the mitral valve and on the septal mitral annulus at the anterior leaflet of the mitral valve. The following parameters were measured: lateral mitral annular systolic velocity ($SmLV_{lat}$), lateral mitral early and late diastolic velocity ($EmLV_{lat}$ and $AmLV_{lat}$), septal mitral annular systolic velocity ($SmLV_{sept}$) and septal mitral early and late diastolic velocity ($EmLV_{sept}$ and $AmLV_{sept}$). Systolic and diastolic tricuspid valve lateral annular velocities were measured, by an analogous method, over the anterior leaflet in the long-axis view of the right ventricle: lateral tricuspid annular systolic velocity ($SmRV_{lat}$) and lateral tricuspid early and late diastolic velocity ($EmRV_{lat}$ and $AmRV_{lat}$). The ratio of early transmitral peak velocity (E) to $EmLV_{lat}$ ($E/EmLV_{lat}$) was used as an approxi-

mation of mean left atrial pressure. Additionally, the average of lateral and septal Em velocities and the E/$EmLV_{aver}$ ratio were measured [11]. Furthermore, the isovolumetric contraction time (IVCT), isovolumetric relaxation time (IVRT) and ejection time (ET) for the lateral and septal mitral as well as the lateral tricuspid annuli were also measured. The myocardial performance index (MPI) was calculated as (IVCT + IVRT)/ET of the examined annuli [12]. All parameters were calculated as the mean of measurements taken in 3 consecutive cardiac cycles. LV diastolic dysfunction was defined as $EmLV_{lat}$ <8 cm/s [13].

Biochemical Parameters

On the day of the echocardiographic examination, the following laboratory parameters were recorded for all patients: serum creatinine concentration, eGFR evaluated by the modified Modification of Diet in Renal Disease (MDRD) formula, serum levels of urea, parathormone (PTH) and hemoglobin (Hb). Additionally, N-terminal of prohormone brain natriuretic peptide (NT-proBNP) levels were measured by immunoassay with the Stratus® CS Acute Care™ Diagnostic System (Siemens). CKD was diagnosed in subjects with an eGFR <60 ml/min/1.73 m^2 according to the NKF-KDOQI [14]. The urinary albumin-to-creatinine ratio was not a subject of our study.

The patients with CKD were divided into two groups according to their eGFR: group 1 with moderate renal dysfunction (30 ≤ eGFR < 60 ml/min/1.73 m^2; 41 patients) and group 2 with severe renal dysfunction (eGFR <30 ml/min/1.73 m^2; 29 patients).

Subsequently, the CKD patients were divided into two other groups according to their $EmLV_{lat}$: a group with diastolic dysfunction (DD group; $EmLV_{lat}$ <8 cm/s; 36 patients) and a group without diastolic dysfunction (WDD group; $EmLV_{lat}$ ≥8 cm/s; 34 patients).

Statistical Analysis

Values of parameters with a normal distribution are presented as means ± standard deviations (SD), whereas values with nonnormal distributions are expressed as medians and ranges. One-way analysis of variance was used to compare continuous variables, and a χ^2 test was used for categorical variables. Pearson's or Spearman's correlation tests were used for correlations between variables. A value of $p < 0.05$ was considered to indicate statistical significance. Receiver operating characteristic (ROC) analysis curves served to determine the optimal cutoff points for identifying patients with LV diastolic dysfunction. In order to determine the diagnostic value of the evaluated parameters, univariate and multivariate logistic regression analyses were employed. To assess the diagnostic value, the OR for particular laboratory and echocardiographic parameters was calculated.

All patients consented in writing to being included in the study. The study protocol was approved by the local bioethics committee (No. 555/2011).

Results

The study included 70 patients with CKD at stages 3–5 (31 males and 39 females with a mean age of 66.6 ± 12.2 years). The following CKD stages were differentiated: stage 3A – eGFR 45–59 ml/min/1.73 m^2 (16 patients); stage 3B – eGFR 30–44 ml/min/1.73 m^2 (25 patients); stage 4 – eGFR 15–29 ml/min/1.73 m^2 (21 patients), and stage 5 – eGFR <15 ml/min/1.73 m^2 (8 patients). The CKD patients were divided into two groups: group 1 consisted of 41 patients with CKD at stages 3A and 3B, and group 2 consisted of 29 patients with CKD at stages 4 and 5. Furthermore, there was a control group of 26 patients without CKD.

The patients and the controls did not differ in age, sex, presence of arterial hypertension and values of systolic and diastolic blood pressure (SBP and DBP). Patients in group 2, as compared to patients in group 1 and the control group, manifested higher values of creatinine, urea and PTH as well as lower values of eGFR. Patients in group 2 compared to patients in group 1 and patients in group 2 compared to the control group were characterized by higher NT-proBNP concentrations, whereas the Hb concentrations were statistically higher in the control group than in groups 1 and 2. In standard echocardiography, CKD patients did not differ in LVEDD, RVEDD, LAD, MAPSE and TAPSE from the control group. Patients in

Table 1. General characteristics of the study population

Parameter	Control group (n = 26)	Group 1 (n = 41)	Group 2 (n = 29)	p
Male gender, n (%)	9 (35)	17 (41)	14 (48)	n.s.
Age, years	63.4±11.3	67.4±14.2	67.8±10.7	n.s.
Hypertension, n (%)	18 (69)	35 (85)	23 (79)	n.s.
SBP, mm Hg	132 (120–145)	140 (120–160)	140 (110–160)	n.s.
DBP, mm Hg	80 (70–95)	90 (70–95)	80 (70–100)	n.s.
Creatinine, mg/dl	0.79 (0.68–1.13)	1.43 (1.02–1.98)	2.95 (1.79–6.31)	<0.0001[a–c]
eGFR, ml/min/1.73 m^2	80±12.9	42.4±8.5	18.2±6.5	<0.0001[a–c]
Urea, mg/dl	34.5±9.9	53.3±13.5	111.3±37.2	<0.0001[a–c]
Hb, g/dl	13.9±1.2	12.9±1.4	11.9±1.9	n.s.[a]; 0.0001[b]; 0.024[c]
log_{10} PTH, pg/ml	1.64±0.14	1.77±0.21	2.23±0.22	0.0001[a, b]; 0.042[c]
log_{10} NT-proBNP, pg/ml	2.01±0.44	2.25±0.35	2.7±0.46	0.0003[a]; 0.0001[b]; n.s.[c]
LVEDD, cm	4.4 (3.8–5.8)	4.7 (4.0–6.1)	4.7 (3.7–6.0)	n.s.
RVEDD, cm	2.7 (2.1–3.0)	2.7 (2.2–3.3)	2.7 (2.2–3.3)	n.s.
LAD, cm	3.8±0.5	4.1±0.5	4.1±0.4)	n.s.
IVSDd, cm	1.0 (0.7–1.4)	1.1 (0.9–1.5)	1.2 (0.9–1.5)	n.s.[a]; 0.005[b]; n.s.[c]
LVPWd, cm	1.0 (0.7–1.5)	1.1 (0.9–1.5)	1.2 (1.0–1.4)	n.s.[a]; 0.0007[b]; n.s.[c]
LVEF, %	60 (51–68)	59 (50–76)	58 (53–71)	n.s.[a]; 0.034[b]; n.s.[c]
LVMI, g/$m^{2.7}$	39.4 (28.4–93)	46 (26.2–90)	50.3 (32–91)	n.s.[a]; 0.015[b]; n.s.[c]
LVFS, %	31 (24–38)	31 (22–38)	30 (22–40)	n.s.
E, cm/s	68 (53–93)	64 (44–120)	58 (35–100)	n.s.
A, cm/s	70 (51–111)	83 (50–118)	82 (47–146)	n.s.[a]; 0.013[b]; 0.02[c]
DT, ms	216±45	224±50	246±67	n.s.
E/A ratio	1.0 (0.6–1.5)	0.8 (0.5–1.9)	0.7 (0.4–1.3)	0.05[a]; <0.0001[b]; n.s.[c]
MAPSE, mm	13.5 (11–17)	13 (11–16)	13 (11–17)	n.s.
TAPSE, mm	23±3	25±3	24±3	n.s.

Values denote means ± SD or medians with ranges in parentheses unless specified otherwise. Group 1: 30 ≤ eGFR < 60 ml/min/1.73 m^2; group 2: eGFR <30 ml/min/1.73 m^2. n.s. = No significance. [a] Group 1, group 2. [b] Group 2, control group. [c] Group 1, control group.

group 2 had significantly higher IVSDd, LVPWd and LVMI as well as lower LVEF than subjects in the control group. The analysis of mitral inflow by pulsed-wave Doppler was as follows: CKD patients did not differ from the control group in velocities of E and DT of the E wave. Velocities of the A wave were significantly higher in groups 1 and 2 than in the control group, whereas they did not differ between the CKD groups. The E/A ratio was lower in group 2 than in the control group and gained borderline significance between groups 1 and 2 (table 1).

Parameters obtained with tissue Doppler imaging (TDI) for all groups are presented in table 2. $SmLV_{lat}$ was higher in group 2 than in group 1 (p = 0.04), whereas $SmLV_{sept}$ was similar for all groups. $EmLV_{lat}$ and $EmLV_{sept}$ were significantly lower in group 2 than in the control group [6 (3–13) vs. 9 (5–14) cm/s, p = 0.015, and 6 (3–12) vs. 7 (4–10) cm/s, p = 0.03, respectively], as was $EmLV_{aver}$ [6 (3.5–12.5) vs. 8 (5–11.5) cm/s, p = 0.008]. These velocities did not differ between groups 1 and 2 as well as between group 1 and the control group.

Late diastolic velocities (Am) in both annuli were similar in the studied groups. The ratio of Em/AmLV in both septal and lateral annuli was significantly lower in group 2 than in group 1 and significantly lower in group 2 than in the control group. The ratio of $E/EmLV_{lat}$ and $E/EmLV_{aver}$ did not differ significantly between the groups. Also the systolic and diastolic velocities of the tricuspid annulus and the ratio of $Em/AmRV_{lat}$, as well as the MPI obtained by TDI and IVRT, IVCT and ET, did not vary significantly between the studied groups.

Table 2. Parameters obtained with TDI for the study groups

Parameter	Control group (n = 26)	Group 1 (n = 41)	Group 2 (n = 29)	p
$SmLV_{lat}$, cm/s	8 (6–14)	7 (5–10)	8 (5–14)	0.04[a]; n.s.[b]; n.s.[c]
$EmLV_{lat}$, cm/s	9 (5–14)	8 (3–14)	6 (3–13)	n.s.[a]; 0.015[b]; n.s.[c]
$AmLV_{lat}$, cm/s	10±2.8	9.5±2.4	11±2.2	n.s.
$Em/AmLV_{lat}$	0.9 (0.3–1.6)	0.9 (0.2–2.2)	0.6 (0.4–1.8)	0.003[a]; 0.006[b]; n.s.[c]
$E/EmLV_{lat}$	7.2 (5.5–13.1)	8.8 (4.7–19.5)	9.0 (4.8–14.2)	n.s.
$SmLV_{sept}$, cm/s	6 (4–9)	6 (4–9)	7 (4–12)	n.s.
$EmLV_{sept}$, cm/s	7 (4–10)	6 (2–11)	6 (3–12)	n.s.[a]; 0.03[b]; n.s.[c]
$AmLV_{sept}$, cm/s	9 (6–13)	9 (5–13)	10 (7–14)	n.s.
$Em/AmLV_{sept}$	0.8 (0.4–1.3)	0.7 (0.3–2.0)	0.5 (0.2–1.2)	0.035[a]; 0.002[b]; n.s.[c]
$EmLV_{aver}$, cm/s	8 (5–11.5)	7.5 (2.5–11)	6 (3.5–12.5)	n.s.[a]; 0.008[b]; n.s.[c]
$E/EmLV_{aver}$	8.7 (5.5–12.6)	9.5 (5.6–24.8)	9.0 (5.1–18.6)	n.s.
$SmRV_{lat}$, cm/s	13 (11–21)	14 (10–20)	14 (8–24)	n.s.
$EmRV_{lat}$, cm/s	12 (9–17)	11 (7–20)	11 (4–20)	n.s.
$AmRV_{lat}$, cm/s	16.9±2.7	16.9±2.9	16.7±4.3	n.s.
$Em/AmRV_{lat}$	0.8 (0.5–1.1)	0.65 (0.45–1.13)	0.7 (0.4–1.1)	n.s.
IVRT LV_{lat}, ms	67 (44–111)	60 (44–122)	67 (40–110)	n.s.
IVCT LV_{lat}, ms	70 (48–120)	70 (44–111)	67 (44–109)	n.s.
ET LV_{lat}, ms	277±27	275±43	272±33	n.s.
MPI LV_{lat}	0.5 (0.35–0.89)	0.46 (0.24–1.11)	0.48 (0.36–0.75)	n.s.
IVRT LV_{sept}, ms	71±16	74±18	79±19	n.s.
IVCT LV_{sept}, ms	67 (44–78)	67 (33–120)	67 (44–111)	n.s.
ET LV_{sept}, ms	288 (216–330)	288 (211–370)	277 (233–360)	0.04[a]; n.s.[b]; n.s.[c]
MPI LV_{sept}	0.47±0.1	0.47±0.1	0.52±0.1	n.s.
IVRT RV_{lat}, ms	55 (40–80)	55 (40–89)	48 (33–78)	n.s.
IVCT RV_{lat}, ms	55 (40–83)	55 (33–90)	50 (33–100)	n.s.
ET RV_{lat}, ms	289±37	290±42	282±42	n.s.
MPI RV_{lat}	0.40±0.07	0.40±0.10	0.37±0.09	n.s.

Values denote means ± SD or medians with ranges in parentheses unless specified otherwise. Group 1: 30 ≤ eGFR < 60 ml/min/1.73 m^2; group 2: eGFR <30 ml/min/1.73 m^2. n.s. = No significance. [a] Group 1, group 2. [b] Group 2, control group. [c] Group 1, control group.

In order to evaluate the echocardiographic changes in CKD patients with LV diastolic dysfunction (defined as $EmLV_{lat}$ <8 cm/s), the patients were divided into two groups depending on their EmLV: the DD group (36 patients) and the WDD group (34 patients) (table 3). Compared to the patients in the WDD group, those in the DD group were characterized by higher NT-proBNP concentrations, LVMI, LVSDd and LVPWd and by lower MAPSE and $SmLV_{lat}$ values.

Logistic Regression Analysis

In order to determine potential and independent parameters indicating LV diastolic dysfunction ($EmLV_{lat}$ <8 cm/s) in CKD patients, univariate and multivariate logistic regression analyses were performed. To assess the diagnostic value, OR for particular parameters were calculated. Only those parameters with $p < 0.1$ in univariate logistic regression were considered (table 4). Among the examined parameters, only MAPSE was found to be an independent predictive factor for LV diastolic dysfunction (OR = 0.39; 95% CI 0.21–0.74, p = 0.003).

ROC Analysis

The area under the ROC curve for MAPSE was 0.801 (95% CI 0.684–0.890, $p < 0.0001$). The optimal cutoff value in the ROC analysis for this parameter was ≤13 mm. This value was

Table 3. Baseline characteristics of the CKD patients in groups with and without LV diastolic dysfunction

Parameter	Whole group (n = 70)	DD group (n = 36)	WDD group (n = 34)	p
Age, years	67.8±12	70.0±11.5	65.2±12.5	0.096
Arterial hypertension, n (%)	59 (84)	31 (86)	28 (82)	0.665
SBP, mm Hg	140 (110–160)	140 (110–160)	140 (120–160)	0.773
DBP, mm Hg	85 (70–100)	80 (70–90)	90 (70–100)	0.186
Body mass index	27.9 (21.3–44.1)	27.5 (21.3–41.9)	29.6 (22.7–44.1)	0.165
Creatinine, mg/dl	1.65 (1.02–6.31)	1.88 (1.02–6.31)	1.61 (1.02–4.31)	0.338
eGFR, ml/min/1.73 m^2	32±14.3	30.6±14.9	34.3±13.5	0.286
Urea, mg/dl	64.5 (20.0–204)	65.5 (30–163)	64.5 (20–204)	0.150
Hb, mg/dl	12.5±1.7	12.5±1.5	12.5±1.9	0.984
$\log_{10}$ PTH, pg/ml	1.96±0.3	1.98±0.3	1.94±0.3	0.587
$\log_{10}$ NT-proBNP, pg/ml	2.46±0.49	2.57±0.55	2.34±0.40	0.050
LVEDD, cm	4.7 (3.7–6.1)	4.7 (3.7–6.1)	4.6 (4.0–5.5)	0.995
RVEDD, cm	2.7 (2.2–3.3)	2.7 (2.2–3.3)	2.7 (2.2–3.3)	0.569
LAD, cm	4.1±0.4	4.1±0.5	4.0±0.4	0.363
LVEF, %	59±5	59±5	60±5	0.548
LVMI, $g/m^{2.7}$	47.7 (26–91)	50.7 (32–91)	43.3 (26.2–77.6)	0.053
IVSDd, mm	11 (9–15)	12 (10–15)	11 (9–15)	0.003
LVPWd, mm	11 (9–15)	12 (9–15)	11 (9–13)	0.045
LVFS, %	30.5±3.5	30.3±3.8	30.8±3.1	0.538
TAPSE, mm	24±3	24±3	24±3	0.863
MAPSE, mm	13 (11–17)	13 (11–17)	14 (11–16)	<0.0001
$SmLV_{lat}$, cm/s	7 (5–14)	7 (5–14)	8 (5–13)	0.006
$SmLV_{sept}$, cm/s	6 (4–12)	6 (4–12)	7 (5–10)	0.131

Values denote means ± SD or medians with ranges in parentheses unless specified otherwise.

Table 4. Echocardiographic and biochemical parameters for the prediction of LV diastolic dysfunction ($EmLV_{lat}$ <8 cm/s) in univariate and multivariate logistic regression analyses

Parameter	Univariate analysis			Multivariate analysis		
	OR	95% CI	p	OR	95% CI	p
Age	1.03	0.99–1.07	0.100	0.99	0.93–1.05	0.665
Arterial hypertension	1.32	0.35–4.95	0.666			
Body mass index	0.94	0.85–1.03	0.183			
Creatinine	1.32	0.84–2.09	0.217			
eGFR	0.98	0.95–1.01	0.283			
Urea	1.01	0.99–1.02	0.117			
Hb	1.00	0.75–1.32	0.983			
$\log_{10}$ PTH	1.55	0.31–7.59	0.581			
$\log_{10}$ NT-proBNP	2.80	0.96–8.15	0.059	2.95	0.56–15.60	0.192
LVEDD	1.17	0.42–3.22	0.748			
RVEDD	1.99	0.23–16.9	0.518			
LAD	1.63	0.56–4.71	0.359			
LVEF	0.97	0.88–1.06	0.542			
LVMI	1.04	1.00–1.08	0.037	0.98	0.91–1.06	0.612
IVSDd	1.76	1.19–2.60	0.004	2.01	0.83–4.86	0.122
LVPWd	1.54	1.01–2.35	0.043	1.02	0.40–2.59	0.963
LVFS	0.95	0.83–1.10	0.535			
TAPSE	1.01	0.86–1.19	0.860			
MAPSE	0.43	0.26–0.70	0.001	0.39	0.21–0.74	0.003
$SmLV_{lat}$	0.71	0.51–0.99	0.042	0.83	0.53–1.30	0.415
$SmLV_{sept}$	0.82	0.58–1.15	0.246			

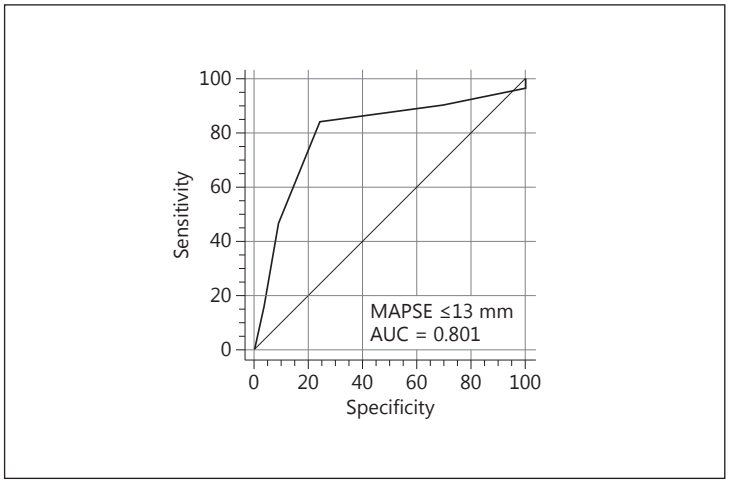

Fig. 1. ROC curve for MAPSE to predict LV diastolic dysfunction.

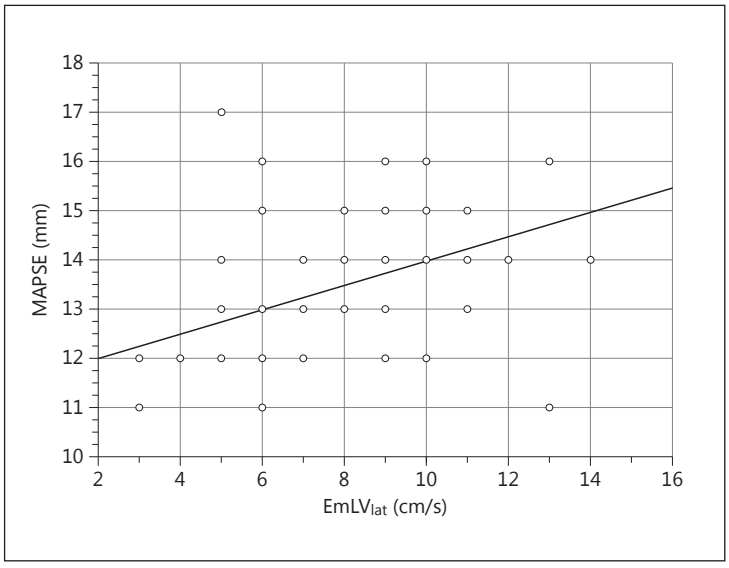

Fig. 2. Positive correlation (r = 0.502, p < 0.0001) between MAPSE level and $EmLV_{lat}$.

characterized by a sensitivity of 84.4% and a specificity of 75.8% for diagnosing LV diastolic dysfunction; the positive predictive value was 77.1% and the negative predictive value 83.3% (fig. 1).

Correlation Analysis

Correlation analysis demonstrated a statistically significant positive correlation between MAPSE level and $EmLV_{lat}$ (r = 0.502, p < 0.0001) (fig. 2).

Discussion

In our study, significant LV diastolic dysfunction appeared only in CKD stages 4 and 5 and rarely accompanied its increased estimated LV end-diastolic filling pressure, which does not confirm earlier reports [15]. In our opinion, CKD patients more frequently develop LV diastolic dysfunction grades I and II, characterized by a decreased or normal E/A ratio with decreased Em velocity, without elevated LV filling pressure.

In our research, patients with severe kidney failure did not differ from non-CKD patients as regards systolic and diastolic tricuspid annular velocities. Thus, we can state that kidney dysfunction does not negatively affect RV function. In our opinion, the presence of CKD does not affect RV function directly and can only have an indirect impact via LV damage and an elevation of LV filling pressure, consequently leading to RV pressure and volume overload. Therefore, in our population of patients, in whom we did not observe increased E/Em values, RV function was normal.

We obtained very interesting results from the analysis of groups with and without LV diastolic dysfunction. Patients in the DD group, as compared to those in the WDD group, were characterized by higher values of LVMI, IVSDd and LVPWd as well as by lower values of MAPSE and $SmLV_{lat}$. LV hypertrophy is characteristic for and well documented in patients with diastolic dysfunction [16, 17]. However, obtaining better results using the M-MODE rather than by TDI was unexpected. Additionally, the only independent variable predicting LV diastolic dysfunction was MAPSE, while SmLV measured on the lateral mitral annulus at the posterior leaflet of the mitral valve was not of statistical significance. In our study, we concluded that the impaired relaxation of the left ventricle resulted in changes in LV systolic function, too. A view supported by other studies is the hypothesis that patients with diastolic dysfunction have a mild impairment in the longitudinal systolic function [18–20]. The LV wall is composed of both circumferentially and longitudinally oriented myocardial fibers. MAPSE is suggested to be primarily representative of subendocardial longitudinal myocardial fibers – compared to the subepicardial, circumferentially oriented fibers measured by LVEF [21]. The systolic diameter reduction in the LV short axis is considered to be caused by the contraction of circumferentially oriented fibers, whereas MAPSE has been shown to be the result of the contraction of longitudinally oriented fibers. This is observed in patients with diastolic dysfunction in whom the long-axis function of the left ventricle measured by MAPSE or SmLV is already impaired while the radial function assessed by LVEF can be still preserved [22, 23]. In our study, MAPSE was more useful than SmLV to detect LV diastolic and systolic dysfunction in patients with CKD. We believe that MAPSE should be proposed as a method for measuring both LV systolic and diastolic functions. The mitral annulus moves down toward the ventricle during systole and up toward the atrium in early diastole and atrial systole, whereas SmLV reflects only the systolic phase.

Bergenzaun et al. [24] have recently showed that MAPSE correlates significantly with markers of LV systolic and diastolic functions as well as with myocardial injury, whereas LVEF does not. In another study, TDI indices of both LV diastolic and systolic functions correlated significantly with MAPSE in patients with diastolic heart failure, illustrating a close relationship between systolic and diastolic LV functions [23]. Additionally, MAPSE obtained better interobserver reproducibility than other traditional and newer measurements of LV systolic function [25].

In our opinion, the influence of MAPSE on LV diastolic dysfunction is complex and difficult to interpret. We believe that differences in the functional importance of cardiac muscle fibers play a significant role here. The function of circumferentially oriented fibers is to ensure a concentric ventricular contraction. However, by becoming thickened during systole, longitudinally oriented fibers ensure that the cavity is fully emptied. Additionally, the contraction of longitudinally oriented fibers affects the motion of fibrous annuli, which consequently leads to the expansion of the atria and them being filled with blood. Thus, it is a decreased MAPSE rather than a reduced LVEF that influences LV diastolic dysfunction [23, 24]. Additionally, LV systolic twisting deformation is one mechanism by which potential energy is stored. After systole, the heart relaxes or untwists – an energy-releasing process – and aids in early LV filling by suctioning [26]. Thus, a decrease in MAPSE will result in less energy being stored during systole and, hence, reduced LV diastolic mechanics. According to Alam et al. [27], the

measurement of MAPSE better reflects diastolic function because, contrary to systolic velocity obtained by TDI, it contains the entire period of the isovolumetric systole.

We conclude that the patients with CKD developed a stepwise reduction in global systolic function and, more importantly, that this happens before the onset of a clinical heart failure. A limitation of this study is that it included a relatively small group of patients from only one center.

Conclusions

A significant reduction of EmLV occurs in CKD stages 4 and 5 and rarely accompanies its increased estimated LV end-diastolic filling pressure, whereas the diastolic function of the right ventricle in these patients seems to be correct. In this study, we showed that reduced MAPSE but not SmLV is an independent predictive factor for LV diastolic dysfunction. Also, we demonstrated that the presence of LV diastolic dysfunction in CKD patients is related to slight impairments of the longitudinal systolic function.

Disclosure Statement

There are no financial or other relationships that could lead to any conflict of interest.

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