Cardiac remodelling and functional alterations in mild-to-moderate renal dysfunction: comparison with healthy subjects

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Introduction

Chronic kidney disease (CKD) is strongly associated with an increased risk of cardiovascular (CV) disease (CVD) and all-cause mortality (Foley et al., 1998; Anavekar et al., 2004; Go et al., 2004). There is an independent, graded association between renal dysfunction and the risks of CVD and death (Anavekar et al., 2004; Go et al., 2004). However, studies investigating the association between mild renal insufficiency and CV risk have shown discordant results (Culleton et al., 1999; Henry et al., 2002; Anavekar et al., 2004; Hosseinpanah et al., 2012).

The increased CV risk in CKD is associated with cardiac remodelling, that is, left ventricular (LV) hypertrophy (LVH) (Foley et al., 1995; Levin et al., 1999; Middleton et al., 2001; Zoccali et al., 2004a). In a cohort of predialysis patients, LVH was the strongest predictor of progression to end-stage renal disease (ESRD) or death (Paoletti et al., 2011). Reduced kidney function is also a risk factor for the development of heart failure (Fried et al., 2003; Kotchen et al., 2007). The risk of CV events in ESRD has been found to be highest in patients with both LVH and reduced LV function (Zoccali et al., 2004b).

Although published data indicate an increasing prevalence of LVH with declining renal function (Levin et al., 1999; Nardi et al., 2009; Chen et al., 2011; Matsumoto et al., 2012), the results regarding early-stage kidney disease are conflicting (Henry et al., 2005; Paoletti et al., 2005). Also, data regarding the association between decline in renal function and LV function are discordant (de Almeida et al., 2007; Edwards et al., 2008; Nardi et al., 2009; Hung et al., 2010; Chen et al., 2011; Liu et al., 2011; Park et al., 2012).

Tissue Doppler imaging (TDI) allows the quantitative evaluation of myocardial function. The technique has an advantage over conventional echocardiography in diagnosing subclinical disease.
abnormalities in systolic and diastolic LV function (Vinereanu et al., 2001; Derumeaux et al., 2002). In advanced CKD, even subclinical signs of diastolic LV dysfunction are associated with worse prognosis (Rakhit et al., 2007; Dogan et al., 2012). Only few studies have evaluated systolic function in CKD using TDI (Hayashi et al., 2006; Edwards et al., 2008; Gulel et al., 2008; Liu et al., 2011).

The aim of our study was to evaluate cardiac structure and function in non-dialysis patients, with different stages of CKD, compared with healthy controls. We were particularly interested to determine whether mild-to-moderate CKD is associated with cardiac remodelling or myocardial dysfunction.

Methods

Patients and control subjects

One hundred three Swedish speaking, non-dialysis patients with CKD, 18–65 years of age, and 53 controls were included in a prospective single-centre observational cohort study, PROGRESS 2002 (Factors impacting progress of renal insufficiency). In the present study, we have analysed the baseline echocardiographic variables in the patients with CKD compared with controls.

Patients were recruited consecutively from the outpatient clinic at the Department of Renal Medicine at the Karolinska University Hospital during 2002–2009 if they had renal function corresponding to stages 2–3 (mild-to-moderate renal dysfunction) or stages 4–5 (severe renal dysfunction) CKD as defined by the National Kidney Foundation (NKF) (National Kidney Foundation, 2002). Patients with known current malignancy were excluded. The patients with CKD were divided into two groups according to glomerular filtration rate (GFR): 49 patients with stage 4–5 CKD (GFR 15.3 ± 3.9 ml min⁻¹ per 1.73 m²) and 54 patients with stage 2–3 CKD (GFR 60.1 ± 5.2 ml min⁻¹ per 1.73 m²). Fifty-three healthy controls (GFR 99.4 ± 12.1 ml min⁻¹ per 1.73 m²), matched for age and sex with the patients with stage 2–3 CKD, were recruited. Of these, 30 were randomly selected from the Swedish Total Population Register and 23 were recruited through the website of the regional university hospital. Interested subjects underwent an interview concerning their health history and medication. Inclusion criteria for the controls were absence of kidney disease, CVD, and diabetes and no ongoing medication.

Before their inclusion in the study, the GFR of all participants was measured by iohexol clearance (Kruzén et al., 1984). After inclusion, all participants underwent clinical investigation, laboratory testing and transthoracic echocardiography (TTE). Exclusion criteria for all participants included kidney transplantation, kidney donation or blood-transmitted disease. One included patient did not complete the baseline echocardiography and was excluded from this study together with her control subject. One of the controls was diagnosed with diabetes after inclusion and was then excluded; meaning that one of the patients with stage 2–3 CKD was without a matched control.

The study protocol was reviewed and approved by the Local Ethics Committee and Institutional Review Board of the Karolinska Institute at the Karolinska Hospital, and all participants gave their written informed consent.

Echocardiography

All ultrasound examinations were performed by two experienced sonographers using an ultrasound machine with a 4-MHz probe equipped with TDI capabilities (Sequoia 512; Siemens Medical Solutions, Mountain View, CA, USA). Two-dimensional, M-mode and Doppler echocardiography were acquired according to the guidelines of the American Society of Echocardiography (ASE) and stored digitally on magneto optical discs and on an EchoPAC server (Image Vault 5.0 system; General Electric Company, Horten, Norway). Heart rate was measured in the supine position during the echocardiography examination. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured in the supine position after the TTE examination was completed.

Standard echocardiographic measurements from the parasternal long-axis view included LV end-diastolic internal dimension (LVIDd), end-diastolic interventricular septal wall thickness (SWTd), end-diastolic LV posterior wall thickness (PWTd) and left atrial end-systolic diameter (LADs). Relative wall thickness (RWT) was calculated as the sum of SWTd and PWTd divided by LVIDd. The mean wall thickness (MWT) of the septal and inferior wall was calculated. LV ejection fraction (LVEF) was calculated from M-mode recordings using the Teichholz method (Teichholz et al., 1976). LV mass (LVM) was obtained using M-mode in the standard parasternal long-axis view and calculated using the formula described by Devereux et al. and recommended by the ASE (Devereux et al., 1986; Lang et al., 2005). LV mass index (LVMI) was calculated as LVM/body surface area (BSA). LVH was defined as LVMI >95 g m⁻² for women and >115 g m⁻² for men, according to ASE recommendations (Lang et al., 2005). In those participants where M-mode images were not acquired in the parasternal long-axis view, LVEF, LVM and LVMI were calculated from 2D images. The measurements of LVEF, LVM and LVMI are presented as the mean of two cardiac cycles. The atrioventricular plane (AV-plane) displacement was measured from M-mode recordings at the mitral annulus adjacent to the anterior, septal, lateral and inferior LV wall using the regional values and the mean value of the four sites of AV-plane displacement of the mitral annulus (Högblund et al., 1988). The AV-plane displacement measurements are presented as the mean of three cardiac cycles.

Transmitral flow velocities were acquired with pulsed Doppler. The velocities of early transmitral diastolic flow velocity (E) and flow velocity during atrial contraction (A), their ratio (E/A ratio), E deceleration time and isovolumic relaxation time (IVRT) were measured. The transmitial
flow velocities are presented as the mean of two cardiac cycles.

**Tissue Doppler imaging**

After completion of the conventional echocardiography, pulsed tissue Doppler imaging was performed. Early diastolic myocardial velocity (e'), late diastolic myocardial velocity (e") and peak systolic myocardial velocity (s') were obtained in the apical four-chamber view and the apical two-chamber view at the septal, lateral, inferior and anterior part of the mitral annulus. A 3-mm sampling volume was used. Mitral e' of the TDI recorded Doppler signal at the septal and lateral part of the mitral annulus was used to calculate the septal (E/e' sept) and lateral (E/e' lat) E/e' ratios. Both values and the mean E/e' ratio (the mean value of E/e' sept and E/e' lat) were used as estimates of the LV filling pressure. The mean of the s' velocities of the four sites was calculated. All TDI variables were measured by two experienced sonographers and are presented as the mean of three cardiac cycles.

**Statistical methods**

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 21.0. (IBM Corp., Armonk, NY, USA). Results are presented as number, percentage, mean and standard deviation (SD). Group comparisons were performed using one-way analysis of variance (ANOVA), Tukey’s post hoc test and chi-square test ($\chi^2$) where applicable. A P value $<$0.05 for a two-tailed test was considered significant.

**Results**

The clinical characteristics of the study participants are summarized in Table 1. The mean age of the participants was 47.7 ± 11.0 years; 60% were men. There were no significant differences between the groups regarding age, sex or body size. There was a significant difference in SBP (P=0.001) and DBP (P = 0.04) only between patients with CKD stages 4–5 and controls.

Echocardiographic findings are summarized in Table 2 and Fig. 1. LVMI ranged from 91 ± 18 g m$^{-2}$, in the controls, to 107 ± 27 g m$^{-2}$ in patients with CKD stages 4–5, and the difference was significant only between CKD 4–5 and controls (P = 0.006). However, there was a significantly higher prevalence of LVH in both CKD groups (CKD 4–5, 37%; CKD 2–3, 30%) compared with the controls (13%); CKD 4–5 versus controls $P = 0.006$, CKD 2–3 versus controls, $P = 0.03$. RWT and MWT were higher in the patients with CKD compared with controls, but the differences were significant only between CKD 4–5 and controls ($P<0.001$ for both RWT and MWT).

There were no significant differences between the groups regarding LV radial systolic function, assessed as LVEF calculated by Teichholz method. However, there was a tendency to higher LVEF in controls (66.0 ± 8.5%) compared with the patients with CKD.

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**Table 1** Characteristics of the study population.

|                     | Controls | CKD 2–3 | CKD 4–5 | $P$ value | $P$ value between groups (post hoc) |
|---------------------|----------|---------|---------|-----------|-----------------------------------|
| No. of patients     | 53       | 54      | 49      |           | NA                                |
| Age (years)         | 47.4 ± 10.7 | 46.8 ± 10.8 | 49.1 ± 11.6 | 0.05     | NA                                |
| Male                | 32 (60–4) | 33 (61–1) | 29 (59–2) | 0.09<sup>a</sup> | NA                                |
| BMI                 | 24.9 ± 3.5 | 25.7 ± 4.9 | 26.0 ± 4.2 | 0.04     | NA                                |
| BSA (m$^2$)         | 1.92 ± 0.19 | 1.92 ± 0.24 | 1.91 ± 0.23 | 0.09     | NA                                |
| Heart rate (beats min$^{-1}$) | 65.2 ± 10.0 | 64.9 ± 13.2 | 64.5 ± 12.5 | 0.09     | NA                                |
| SBP (mmHg)          | 117 ± 12.4 | 123 ± 15.4 | 130 ± 19.8 | $<0.001$ | $<0.001$<sup>b</sup> |
| DBP (mmHg)          | 73 ± 8.9  | 77 ± 10.4 | 78 ± 10.3 | 0.03     | 0.04<sup>b</sup>                  |
| Diabetes            | 11 (20–4) | 7 (14–3) |          | 0.4<sup>a</sup> | NA                                |
| Diagnosis CKD       |          |         |         |           | NA                                |
| Familial/hereditary/congenital diseases | 14 (25–9) | 13 (26–5) |          | 0.09<sup>a</sup> | NA                                |
| Primary glomerulonephritis | 17 (31–5) | 12 (24–5) |          | 0.4<sup>a</sup> | NA                                |
| Secondary glomerular/systemic disease | 9 (16–7) | 10 (20–4) |          | 0.6<sup>a</sup> | NA                                |
| Miscellaneous/unknown | 14 (25–9) | 14 (28–6) |          | 0.8<sup>a</sup> | NA                                |
| Medication          |          |         |         |           | NA                                |
| Diuretics           | 12 (22–2) | 34 (69–4) |          | $<0.001$<sup>a</sup> | NA                                |
| ACE inhibitors      | 23 (42–6) | 29 (59–2) |          | 0.09<sup>a</sup> | NA                                |
| Angiotensin II receptor blockers | 22 (40–7) | 23 (46–9) |          | 0.5<sup>a</sup> | NA                                |
| Beta-blockers       | 11 (20–4) | 20 (40–8) |          | 0.02<sup>a</sup> | NA                                |
| Calcium channel blockers | 10 (18–5) | 28 (57–1) |          | $<0.001$<sup>a</sup> | NA                                |

BMI, body mass index; BSA, body surface area; GFR, glomerular filtration rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; CKD, chronic kidney disease; ACE, angiotensin converting enzyme.

Values reported as number (percentage) or mean ± standard deviation.

<sup>a</sup>Chi-square test.

<sup>b</sup>CKD 4–5 versus controls.
### Table 2  Echocardiographic variables.

|                        | Controls     | CKD 2–3       | CKD 4–5       | P value ANOVA | P value between groups (post hoc) |
|------------------------|--------------|---------------|---------------|---------------|----------------------------------|
| No. of patients        | 53           | 54            | 49            |               |                                  |
| Aortic diameter (cm)   | 2.88 ± 0.33  | 2.94 ± 0.43   | 2.82 ± 0.33   | 0.3           | NA                               |
| LADs (cm)              | 3.38 ± 0.48  | 3.58 ± 0.59   | 3.64 ± 0.62   | 0.05          | NA                               |
| SWTd (cm)              | 0.99 ± 0.16  | 1.09 ± 0.20   | 1.15 ± 0.23   | <0.001        | <0.001a 0.02b                    |
| LVIDd (cm)             | 4.71 ± 0.49  | 4.69 ± 0.60   | 4.65 ± 0.56   | 0.9           | NA                               |
| PWTd (cm)              | 0.99 ± 0.14  | 1.02 ± 0.14   | 1.09 ± 0.19   | 0.002         | 0.002c                           |
| LVM (g)                | 176.2 ± 44.5 | 193.4 ± 68.5  | 207.3 ± 67.6  | 0.04          | 0.03a                            |
| LVM (g m⁻²)            | 91.2 ± 17.6  | 99.7 ± 29.6   | 107.0 ± 27.2  | 0.008         | 0.006a                           |
| LVH                    | 7 (13)       | 16 (30)       | 18 (37)       | 0.02 (all)d   | 0.006b 0.03b                     |
| RWT (cm)               | 0.42 ± 0.07  | 0.46 ± 0.08   | 0.49 ± 0.10   | 0.001         | <0.001a                         |
| MWT (cm)               | 0.99 ± 0.13  | 1.06 ± 0.16   | 1.12 ± 0.20   | <0.001        | <0.001a                         |
| LV systolic function   |              |               |               |               |                                  |
| LVEF Teichholz (%)     | 66.0 ± 8.5   | 62.5 ± 7.6    | 62.2 ± 9.6    | 0.05          | 0.07a 0.09b                     |
| Septal AV (cm)         | 1.43 ± 0.22  | 1.33 ± 0.19   | 1.31 ± 0.19   | 0.008         | 0.01a 0.03b                     |
| Lateral AV (cm)        | 1.56 ± 0.22  | 1.47 ± 0.26   | 1.52 ± 0.30   | 0.2           | NA                               |
| Inferior AV (cm)       | 1.57 ± 0.24  | 1.44 ± 0.25   | 1.44 ± 0.23   | 0.006         | 0.02a 0.01b                     |
| Anterior AV (cm)       | 1.43 ± 0.19  | 1.33 ± 0.25   | 1.34 ± 0.26   | 0.05          | 0.06b                           |
| Mean AV (cm)           | 1.50 ± 0.17  | 1.39 ± 0.20   | 1.40 ± 0.21   | 0.008         | 0.04a 0.01b                     |
| RV systolic function (TAPSE) | 2.47 ± 0.45  | 2.31 ± 0.45   | 2.25 ± 0.40   | 0.03          | 0.03a                            |
| LV diastolic function  |              |               |               |               |                                  |
| E deceleration (ms)    | 206 ± 47     | 203 ± 40      | 213 ± 48      | 0.6           | NA                               |
| E wave velocity (cm s⁻¹)| 73 ± 15      | 74 ± 17       | 80 ± 18       | 0.1           | NA                               |
| A wave velocity (cm s⁻¹)| 54 ± 13      | 58 ± 15       | 69 ± 18       | <0.001        | <0.001b 0.002c                  |
| E/A                    | 1.43 ± 0.39  | 1.33 ± 0.35   | 1.24 ± 0.49   | 0.09          | NA                               |
| IVRT (ms)              | 73 ± 17-3    | 76.6 ± 15.4   | 77.5 ± 15.5   | 0.4           | NA                               |

LADs, left atrium end-systolic diameter; SWTd, wall thickness of interventricular septum; LVIDd, left ventricular end-diastolic dimension; PWTd, posterior wall thickness; LVM, left ventricular mass; BSA, body surface area; LVMi, left ventricular mass/BSA; LVH, left ventricular hypertrophy; RWT, relative wall thickness; MWT, mean wall thickness; LV, left ventricle; LVEF, left ventricular ejection fraction; AV, atrio-ventricular plane displacement; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion; E, early transmitral diastolic flow velocity; A, flow velocity during atrial contraction; IVRT, isovolumic relaxation time.

Values reported as number (percentage) or mean ± standard deviation.

*CKD 4–5 versus controls.

**CKD 2–3 versus controls.

†CKD 4–5 versus CKD 2–3.

‡Chi-square test.

patients with CKD (CKD 4–5, 62.2 ± 6.9%, P = 0.07; CKD 2–3, 62.5 ± 7.6%, P = 0.09). In addition, the controls had significantly higher longitudinal systolic contraction measured as AV-plane displacement in the septal and inferior LV wall, and also a higher mean value of the four sites of AV-plane displacement (1.50 ± 0.17 cm) compared with the patients with CKD (CKD 4–5, 1.40 ± 0.21 cm, P = 0.04; CKD 2–3, 1.39 ± 0.20 cm, P = 0.01). There were no significant differences between the groups regarding traditional variables of diastolic function such as mitral E velocity, the mitral E/A ratio or the mitral E deceleration time.

In a subgroup analysis of patients with CKD 2–3, there were no significant differences in blood pressure or any echocardiographic variables between subjects with GFR ≥ 60 ml min⁻¹ per 1.73 m² and GFR <60 ml min⁻¹ per 1.73 m².

Tissue Doppler imaging variables are summarized in Table 3. The mean value of the systolic TDI velocities of the four sites was significantly higher in controls (11.5 ± 1.9 cm s⁻¹) compared with the control groups (CKD 4–5, 10.4 ± 2.1 cm s⁻¹, P = 0.03 and CKD 2–3, 10.4 ± 2.1 cm s⁻¹, P = 0.02).

Controls had a significantly higher septal $e'$ velocity of 13.6 ± 3.0 cm s⁻¹ compared with both groups of patients with CKD (CKD 4–5, 11.7 ± 2.8 cm s⁻¹, P = 0.002 and CKD 2–3, 11.8 ± 2.5 cm s⁻¹, P = 0.003). In addition, controls had significantly lower mitral $E'/e'$ ratio assessed as the mean $E'/e'$ (5.00 ± 1.23) compared with both groups of patients with CKD (CKD 4–5, 6.36 ± 1.71, P<0.001 and CKD 2–3, 5.69 ± 1.47, P = 0.05), indicating impaired diastolic function in the patients with CKD compared with the controls. Septal $e'/a'$ ratio was significantly lower than controls only for CKD 4–5.

### Discussion

In this study using tissue Doppler imaging, we found significant abnormalities in diastolic and longitudinal systolic LV function in patients with mild-to-moderate CKD compared
groups and controls. Mean AV and those with CKD stages 2
controls. Ling, with a significantly higher prevalence of LVH than in
et al. reported in patients with increasing severity of CKD (Levin
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Global systolic LV function is traditionally measured as LVEF,
calculated from simplistic models using diastolic and systolic
dimensions or volumes of the LV (Lang et al., 2005). Recently, the interaction between the complicated structure
and orientation of myocardial fibres and the contractile LV
function has been clarified (Sengupta et al., 2006). Longitudi-
nal contraction of the left ventricle can be expressed by AV-
plane displacement measured by M-mode or/and systolic
myocardial velocity measured by TDI. In our study, patients
with CKD in both groups had significantly lower systolic
myocardial velocities and lower AV-plane displacement, com-
pared with controls. Recent studies employing a newly devel-
oped ultrasound-based strain imaging technique confirm our
results in terms of impairment of longitudinal systolic func-
tion in patients with CKD (Edwards et al., 2008; Liu et al.,
2011). We did not find any statistically significant differences
between the groups in LVEF calculated by the Teichholz
method.

Development of TDI imaging has also influenced the evalua-
tion of diastolic LV function, adding variables calculated from
transmitral flow and myocardial velocities. Park et al. (2012)
did not find any graded association between kidney function
and diastolic LV function assessed by traditional methods.
However, they did not use TDI for the assessment of diastolic
function and they did not have a healthy control group for
comparison. In our study, we did not see any significant
differences between the groups regarding traditional character-
istics of transmitral inflow pattern (E/A ratio) or left atrial

Figure 1  Box plots presenting comparisons of systolic (Mean AV and Mean e’) and diastolic (Septal e’ and Mean E/e’) variables between the CKD

groups and controls. Mean AV – mean value of the atrio-ventricular plane displacement at the four sites of the mitral annulus, Mean e’ – mean
value of peak systolic myocardial velocities of the four sites of the mitral annulus, Septal e’ – the early diastolic myocardial velocity of the sepal
part of the mitral annulus, Mean E/e’ – the mean value of the ratio between the velocity of early transmitral diastolic flow velocity (E) and the
early diastolic myocardial velocity (e’) of the septal and lateral part of the mitral annulus.

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| Table 3 | Tissue Doppler imaging. |
|---------|-------------------------|
|         | Controls | CKD 2–3 | CKD 4–5 | P value ANOVA | P value between groups (post hoc) |
| No. of patients | 53       | 54       | 49       |              |                                 |
| Septal $'\prime$ (cm s$^{-1}$) | 9.4 ± 1.2 | 8.9 ± 1.3 | 9.1 ± 1.6 | 0.2 | NA |
| Septal $'\prime$ (cm s$^{-1}$) | 13.6 ± 3.0 | 11.8 ± 2.5 | 11.7 ± 2.8 | 0.001 | 0.002$^a$ 0.003$^b$ |
| Septal $a'$ (cm s$^{-1}$) | 11.9 ± 2.1 | 11.4 ± 1.6 | 13.1 ± 3.1 | 0.001 | 0.001$^a$ 0.02$^b$ |
| Septal $e'$ ratio | 1.21 ± 0.45 | 1.06 ± 0.30 | 0.936 ± 0.31 | 0.001 | 0.001$^a$ |
| Lateral $'\prime$ (cm s$^{-1}$) | 12.4 ± 2.8 | 11.2 ± 3.7 | 10.7 ± 2.9 | 0.02 | 0.02$^a$ |
| Lateral $a'$ (cm s$^{-1}$) | 17.6 ± 4.9 | 15.6 ± 4.5 | 15.0 ± 4.9 | 0.02 | 0.02$^a$ |
| Lateral $e'$ (cm s$^{-1}$) | 11.7 ± 2.8 | 11.5 ± 3.3 | 12.0 ± 3.0 | 0.7 | NA |
| Lateral $e'/a'$ ratio | 1.63 ± 0.77 | 1.44 ± 0.52 | 1.35 ± 0.64 | 0.09 | NA |
| Mean $e'$ (cm s$^{-1}$) | 1.42 ± 0.57 | 1.25 ± 0.36 | 1.14 ± 0.45 | 0.01 | 0.01$^a$ |
| Inferior $'\prime$ (cm s$^{-1}$) | 10.9 ± 1.6 | 10.2 ± 1.3 | 10.2 ± 1.7 | 0.02 | 0.04$^a$ 0.05$^b$ |
| Inferior $a'$ (cm s$^{-1}$) | 15.4 ± 3.8 | 14.3 ± 3.6 | 13.6 ± 4.5 | 0.07 | NA |
| Inferior $e'$ (cm s$^{-1}$) | 13.1 ± 2.2 | 12.3 ± 2.2 | 13.6 ± 3.7 | 0.06 | NA |
| Anterior $'\prime$ (cm s$^{-1}$) | 13.2 ± 5.1 | 11.2 ± 4.0 | 11.6 ± 4.2 | 0.07 | NA |
| Anterior $a'$ (cm s$^{-1}$) | 17.5 ± 5.0 | 15.4 ± 5.2 | 14.3 ± 4.0 | 0.003 | 0.003$^a$ |
| Anterior $e'$ (cm s$^{-1}$) | 12.9 ± 5.6 | 11.3 ± 3.1 | 12.6 ± 4.0 | 0.2 | NA |
| Mean $e'$ (cm s$^{-1}$) | 11.5 ± 1.9 | 10.4 ± 2.1 | 10.4 ± 2.1 | 0.01 | 0.03$^a$ 0.02$^b$ |
| E/e' sept | 5.59 ± 1.38 | 6.39 ± 1.64 | 7.12 ± 2.26 | <0.001 | <0.001$^a$ |
| E/e' lat | 4.41 ± 1.26 | 4.99 ± 1.62 | 5.60 ± 1.55 | 0.001 | <0.001$^a$ |
| Mean E/e' | 5.00 ± 1.23 | 5.69 ± 1.47 | 6.36 ± 1.71 | <0.001 | <0.001$^a$ 0.05$^b$ |

$'\prime$, peak systolic myocardial velocity; $e'$, early diastolic myocardial velocity; $a'$, late diastolic myocardial velocity; mean $e'$, mean value of peak systolic myocardial velocity of the septal, lateral, inferior and anterior part of the mitral annulus; E, early transmitral diastolic flow velocity; sept, septal part of the mitral annulus; lat, lateral part of the mitral annulus; mean E/e', mean value of E/e' sept and E/e' lat.

Values reported as number or mean ± standard deviation.

$^a$CKD 4–5 versus controls.

$^b$CKD 2–3 versus controls.

$^C$CKD 4–5 versus CKD 2–3.

size. However, when TDI was used, the patients with CKD in both groups had significantly lower septal diastolic velocity ($e'$) and higher mitral mean E/e' ratio compared with the controls, indicating an impairment of diastolic function in the patients with CKD, although the majority had preserved LVEF. These changes in diastolic variables may be precursors of clinical heart failure. Devereux et al. (2000) showed that the patients with renal dysfunction are more likely to have heart failure with preserved LVEF. Our findings are consistent with previous studies showing that TDI is a more sensitive tool than conventional echocardiography for the detection of impaired diastolic function in the patients with CKD (Hayashi et al., 2006; de Almeida et al., 2007).

There are some study limitations. The sample size is relatively small. We were not able to ascertain the duration of comorbid conditions, such as hypertension and diabetes.

Conclusion

Alterations in systolic and diastolic myocardial function, compared with healthy subjects, can be seen in patients with even mild-to-moderate CKD when TDI is used. Traditional echocardiographic measures of diastolic function did not show any significant differences. There was also an increasing prevalence of LVH with increasing severity of CKD. Our findings indicate that cardiac involvement is already present in mild-to-moderate CKD and may be a precursor of premature cardiac morbidity.

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The authors declare that they have no financial interests.

Conflict of interest

The authors declare no conflict of interest.
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