Cukurova Medical Journal
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

Cukurova Med J 2020;45(3):1089-1098
DOI: 10.17826/cumj.661790

ARAŞTIRMA / RESEARCH

Abnormal geometry and hypertrophy of left ventricle in patients with chronic kidney disease

Kronik böbrek hastalarında anormal kalp geometrisi ve sol ventrikül hipertrofisi

Bülent Kaya[1], Saime Paydaş[1], Neslihan Seyrek[1], Mustafa Balal[1], İbrahim Karayaylalı[1]

[1]Çukurova Üniversitesi Tıp Fakültesi Nefroloji Bilim Dalı, Adana, Turkey

Cukurova Medical Journal 2020;45 (3):1089-1098

Abstract

Purpose: The aim of this study was to investigate the incidence of left ventricular geometric patterns in patients with chronic kidney disease (CKD).
Materials and Methods: A total of 162 patients (100 males) with stage 2–5 CKD were included in the study. Patient age was between 17 and 79 years. Left ventricular geometry (LVG) patterns were calculated as left ventricular normal geometry (LVNG), left ventricular concentric remodeling (LVCR), concentric left ventricular hypertrophy (cLVH) and eccentric left ventricular hypertrophy (eLVH) by echocardiographic parameters.
Results: The incidence of LVH was 45.1%. LVG patterns were found as follows: eLVH in patients 18(11.1%), cLVH in 42(25.9%), LVCR in 51(31.5%), and LVNG 51(31.5%). LVNG was found 10.38% and 34.27% in CKD stage 2 and dialysis, respectively. LVCR was as high as 62.3% in CKD stage2. cLVH and eLVH were found as 35.92% and 29.13% in stage 5 non-dialysis and dialysis, respectively. There was a relationship between clinical characteristics and LVG as follows age and GFR with LVCR, HbA1C and serum levels of albumin and sodium with cLVH, and age and serum albumin with eLVH
Conclusions: In our CKD patients, abnormal LVG was found as earlier as CKD stage 2. The incidence of cLVH and eLVH was higher in advanced stages of CKD. Nontraditional factors such as volume status and nutrition were also crucial for left ventricular remodeling.
Keywords:. Left ventricular geometry, left ventricular hypertrophy, chronic kidney disease

Öz

Amaç: Bu çalışmanın amacı kronik böbrek hastalığı (KBH) olan hastalarda sol ventrikül geometrisi (SVG) çeşit ve sıklığını araştırmaktır.
Gereç ve Yöntem: Evre 2-5 KBH'lı, yaşı 17-79 aralığında, 100'ü erkek toplam 162 hasta çalışmaya dahil edildi. SVG ekokardiyografik parametrelere göre; sol ventrikül normal geometrisi (SVNG), sol ventrikül konsantrik remodelling (SVKR), konsatrik sol ventrikül hipertrofisi (SVKH) ve eksantrik sol ventrikül hipertrofisi (ESVH) olarak hesaplandı.
Bulgular: Hastalarımızda SVH sıklığı % 45.1 idi. SVG paternleri: ESVH 18 (% 11.1), KSVH 42 (% 25.9), SVKR 51 (% 31.5) ve SVNG 51 (% 31.5) saptandı. SVNG evre 2 KBH ve diyaliz hastalarında sırasıyla %10.38 ve %34.27 idi. SVKR, evre 2 KBH'da yüksek sıklıkta (% 62.3) saptandı. Non-diyaliz evre 5 KBH ve diyaliz hastalarında KSVH ve ESVH sıklığı sırasıyla % 35.92 ve % 29.13 bulundu. Klinik özellikler ile SVG değerlendirildiğinde; yaş ve GFR SVKR ile, HbA1C, serum albumin ve sodyum seviyeleri KSVH ile, yaş ve serum albumin ESVH ile ilişkiliydi.
Sonuç: KBH hastalarımızda, evre 2 KBH aşamasında bile anormal SVG saptandı. KBH'ın ileri evrelerinde KSVH ve ESVH insidansı daha yüksekti. Volum durumu ve beslenme gibi geleneksel olmayan faktörler de sol ventrikül yeniden şekillenmesinde önemliydi.

Anahtar kelimeler: Sol ventrikül geometrisi, sol ventrikül hipertrofisi, kronik böbrek hastalığı

INTRODUCTION

Cardiovascular disease (CVD) is a leading cause of death in chronic kidney disease (CKD) patients, in whom mortality is 20–30 times higher than in the general population[1]. The increased risk cannot be attributed only to conventional cardiovascular risk factors, such as advanced age, smoking, hypertension

Yazışma Adresi/Address for Correspondence: Dr. Bülent Kaya, Çukurova Üniversitesi Tıp Fakültesi Nefroloji Bilim Dalı, Adana, Turkey, E-mail: bulentkaya32@gmail.com
Geliş tarihi/Received: 19.12.2020 Kabul tarihi/Accepted: 13.06.2020 Çevrimiçi yayın/Published online: 30.08.2020

(HTN), hyperlipidemia, and diabetes mellitus (DM). Other risk factors such as inflammation, hypervolemia, malnutrition, anemia, secondary hyperparathyroidism (SHPT), oxidative stress, and bone mineral disorders also play a role in CKD patients[2-5]. Left ventricular hypertrophy (LVH) and left ventricular mass index (LVMI) are independent predictors of cardiovascular mortality in CKD patients[6-8]. Many factors play a role in the development of LVH in CKD patients, including anemia, HTN, hyperphosphatemia, SHPT, chronic volume overload, and inflammation[6,9,10]. LVH prevalence has been reported as 30-70% in CKD patients and 70% at the beginning of dialysis[11]. LVH is generally a prognostic marker and is an independent risk factor for arrhythmia, sudden death, cardiac failure, myocardial ischemia, post-transplant the major cardiovascular event, and early graft failure[6,12].

The left ventricular mass (LVM) is divided into four categories according to the geometric pattern. Normal LVM is divided into two subgroups, being left ventricular normal geometry (LVNG) and left ventricular concentric remodeling (LVCR), while increased LVM is evaluated in two groups as concentric LVH (cLVH) and eccentric LVH (eLVH). The relative wall thickness (RWT) is increased when compared to the left ventricular cavity in patients with cLVH, while this is not the case for patients with eLVH[13]. Abnormalities associated with left ventricular geometry (LVG) are seen frequently in CKD patients[14]. cLVH is more common in with predialysis CKD patients, and eLVH is more common in dialysis patients[11,15-17]. LVG changes over time and the progression of CKD[17,18]. Both geometric patterns are associated with increased CVD risk, while the risk of sudden death is five-fold in patients with eLVH when compared to cLVH in undergoing dialysis patients[16,19].

Therefore, detection and prevention of factors affecting LVG in CKD patients are vital in reducing the risk of CVD. In this cross-sectional study, we evaluate the frequency of LVH and LVG patterns, and the affecting factors, in 162 patients with CKD stage 2–5.

MATERIALS AND METHODS

All procedures were performed in the study were in accordance with the ethical standards of the Helsinki Declaration. Informed consent was obtained from all patients included in the study. This study has been approved by the ethics committee of the Cukurova University Faculty of Medicine (31.08.2018, 80/32).

Patients between 18-80 years old, CKD stage 2 and above, who applied to our Nephrology outpatient clinic were included in our study. Patients with class 3–4 congestive heart failure, chronic liver disease, acute infection, acute coronary syndrome, history of renal transplantation, obesity (BMI≥35 kg/m^2), malignancy, and patients who declined to give consent were excluded from the study. Two hundred patients were included in our study, but 38 patients were excluded because of exclusion criteria. The remaining 162 patients were included in our study.

Procedure

Height, weight, body mass index (BMI), Blood Pressure (BP) and physical examination findings of the patients were recorded. Office BP was measured two times with 3 minutes interval using a mercury sphygmomanometer while the patient was in a sitting position in a quiet room. All patients were asked to avoid caffeinated drinks, alcohol, tobacco products, for 30 minutes before the measurements. Patients with office BP>140/90 mmHg or treated with the anti-hypertensive drug(s) were accepted as hypertensive. BMI was calculated based on height and weight measurements (kg)/height^2(meter^2).

Biochemical evaluations

Blood samples were drawn in the morning following a fasting period of 12 hours. Biochemical tests, including glucose, BUN, creatinine, uric acid (UA), sodium (Na), potassium (K), calcium (Ca), phosphorus (P), albumin, HDL, LDL, triglyceride, ferritin, HbA1c, parathormone (PTH), 25 OH Vitamin D, Fibroblast growth factor 23 (FGF23), C-reactive protein (CRP) and whole blood count were measured. Glomerular filtration rate (eGFR) was calculated using the MDRD formula[20]

Of the study sample, 16 patients were undergoing four hours of hemodialysis (HD) three times a week, involving treatment with a dialysate solution of 2.0 mmol/l K^+, 1.25 mmol/l Ca^{2+}, 138 mmol/l Na^+ and 0.5 mmol/l Mg^{2+}. Standard (conventional) PD solutions (Baxter Healthcare, Deerfield, IL, USA, and Fresenius Medical Care, Germany) were used on 29 patients undergoing peritoneal dialysis (PD) treatment.

Biochemical parameters were measured

Roche/Hitachi 912/917/MODULAR. 25 OH Vitamin D was measured using HPLC (High-pressure liquid chromatography). The FGF23 level was measured using an Enzyme-Linked Immunosorbent Assay (ELISA) using a commercial kit (USCN Life Science Inc. Wuhan, China).

Echocardiographic measurements

The examination was performed with two-dimensional echocardiography (ACUSON SC 256 machine with a transducer 3.5 MHz). HD patients were examined 2 to 24 hours after the last HD session. The echocardiographic technique, calculation of dimensions, and different cardiac volumes were realized according to recommendations of the American Society and European Association of Echocardiography. The echocardiographic evaluation included endocavitary dimensions of the left ventricle and other cardiac chambers. The LVM was calculated according to Devereux formula[21]: 1.04 × (LVID + PWT + IVST)3 - LVID3× 0.8 + 0.6 where LVID indicates left ventricular internal diameter; PWT, posterior wall thickness; and IVST, intraventricular septal thickness. LVH was determined as LVMI higher than 115 g/m² for men and greater than 95 g/m² for women. The relative wall thickness (RWTH) was calculated as PWT plus IVST, divided by the LVID; the limit value was considered 0.42 and greater.

According to LVM and RWTH, the prevalence of 4 geometrical models of the left ventricle was evaluated for the patients: LVNG (LVMI, ≤ 95 g/m² for women and ≤ 115 g/ m² for men; RWTH, ≤ 0.42); LVCR (LVMI ≤ 95 g/m² for women and ≤ 115 g/ m² for men; RWTH, > 0.42); cLVH (LVMI > 95 g/m² for women and > 115 g/ m² for men; RWTH, > 0.42); eLVH (LVMI > 95 g/m² for women and > 115 g/ m² for men; RWTH, ≤ 0.42)[13].

Statistical analysis

The data were analyzed using the SPSS 19.0 program (IBM, Chicago IL. USA). Categorical measurements were done using number and percentage; numerical measurements were done using average and standard deviation (when appropriate median and minimum-maximum). Student T-test, Mann witney U test, and chi-square test were used to compare groups with and without LVH. The Tukey test was used to determine the difference between the groups.

The multinomial logistic regression model assessed the relationship between LVG patterns. To estimate the predictors of different geometric models, a multinomial logistic regression analysis was performed with normal geometry as the reference category. Age, SBP, GFR, hgb, albumin, Na, P, CaxP, PTH, FGF23, HbA1C, LDL, and CRP were included as covariates. The covariates of the multinational logistic regression model were selected based on their importance in univariate analyzes, potential confounding factors based on the comparison of groups with and without LVH, and literature reviews. Statistical probability was used as 0.05 in all the tests.

RESULTS

A total of 162 patients in our study were divided into five groups according to CKD stages: 17 stages two patients, 38 stages three patients, 39 stages four patient, 23 stages five patient in the non-dialysis (5ND), and 45 dialysis patient (5D). Among the 5D group, 16 patients were receiving HD, and 29 were receiving PD treatments.

The causes of CKD were diabetic nephropathy in 58 patients, chronic glomerulonephritis in 14, polycystic kidney disease in 13, nephrolithiasis in 10, hypertensive nephrosclerosis in 9 and other causes in 19 patients, while the cause of CKD was unknown in 39 patients. Of the total study sample, 81 were cigarette smokers, while 22 were alcohol consumers. Demographic and clinical data of the patients are presented in table 1. The rate of LVH was found to be 51/117 (43.6%), 22/45 (48.9%), and 73/162 (45.1%) in predialysis, dialysis, and the whole series, respectively. Frequency of LVH by stage were 3/17 (17.6%), 12/38 (31.6%), 22/39 (56.4%), 14/23 (60.9%) and 22/45 (48.9%) in stage 2, stage 3, stage 4, 5ND and 5D, respectively.

cLVH and eLVH were identified in 42/73 (%57.5) and 18/73 (24.6%) of the patients with LVH, respectively. The LVG patterns were shown in Figure 1. The rate of LVNG was found to be the lowest in CKD stage 2 (10.38%) and the highest in 5D (34.27%).

Table 1. Demographic and clinical characteristics of chronic kidney disease patients (n=162)

Parameters	Stage 2 (n=17)	Stage 3 (n=38)	Stage 4 (n=39)	Stage 5ND (n=23)	Stage 5D (n=45)	p
Age, years	61.2±10.8	56.9±10.7	51.3±13.2	47±13	47.9±15.2	<0.001*,0.007c, 0.004d,0.035f,0.016 g
BMI, kg/m²	28.8±3.8	27.5±3.2	27.9±4.2	25.9±4.7	25.7±4.6	0.020*
SBP, mmHg	125.3±16.2	134.1±16.7	132.8±18.2	136.1±18.5	136.2±19.9	0.294
DBP, mmHg	73.5±7	80.5±10.6	83.1±10.2	83.5±11.4	83.2±10.3	0.011*, 0.014b, 0.024c, 0.01d
BP≥140/90 mmHg, n(%)	3(17.6)	18(47.4)	17(43.6)	10(43.5)	25(55.6)	0.121*,0.059d
HTN, n(%)	14(82.4)	36(94.7)	37(94.9)	20(87)	35(77.8)	0.086*
Anti-HT drug, n(%)	13(76.5)	32(84.2)	35(89.7)	20(87)	30(66.7)	0.071*
ACEI, n(%)	7(41.2)	11(28.9)	6(15.4)	3(13)	3(6.7)	0.008*, 0.014d
ARB, n(%)	5(29.4)	10(26.3)	7(17.9)	3(13)	3(6.7)	0.101*
Beta blocker, n(%)	3(17.6)	11(28.9)	18(46.2)	11(47.8)	15(33.3)	0.160*
CCB, n(%)	5(29.4)	14(36.8)	19(48.7)	13(56.5)	23(51.1)	0.316*
Phosphour binders, n(%)	0	0	3(7.7)	7(30.4)	28(62.2)	<0.001*,d,g,j, 0.046c, 0.003k
Calcitriol, n(%)	0	3(7.9)	4(10.3)	12(52.2)	23(51.1)	<0.001*,s,d,f,g,j, 0.001h
CKD time (month)	10.6±2.6	33.3±28.1	35.2±28.5	55.0±54	49.8±34.4	<0,001*,c,d
eGFR, ml/min/1.73m²	70.2±7.8	42.9±7.8	22.0±3.3	11.4±3.0	7.0±3.7	<0.001*,a,b,c,d,e,f,g,h,j, 0.015k
DM, n (%)	11(64.7)	18(47.4)	13(33.3)	6(26.1)	10(22.2)	0.011*, 0.014d
FGF23, pg/ml	8.2(5.6-11.3)	10.4(4.2-42.1)	16.2(3-86.2)	10.4(4.1-31.3)	10.4(5.1-190)	0.145*
Hgb, g/dl	12.4±1.8	13.3±2.1	11.7±1.6	10.7±1.7	10.7±1.5	<0.001*,f,g, 0.036c 0.014d, 0.002e
Ferritin, ng/ml	77.4(19-267)	29.6(6-669)	57.3(9-387)	111.9(18-993)	316.8(10-1075)	<0.001*,d,g,j,k
Glucose, mg/dl	171.5±99.6	119.7±43.2	106.8±38.8	130.5±83	98.9±25.6	<0.001*, 0.012a 0.001b, <0.001d
Creatinine, mg/dl	0.9±0.2	1.6±0.3	2.7±0.6	5.3±1.8	8.7±2.6	<0.001
Albumin, g/dl	3.6±0.5	3.9±0.5	3.6±0.5	3.4±0.7	3.4±0.6	0.001*, 0.011f <0.001g
Sodium, mmol/l	135.6±2.7	136.3±3.4	135.8±2.9	136.1±3.1	134.8±3.2	0.257
Phosphorus, g/dl	3.7±0.5	3.6±0.8	3.8±0.7	4.9±1.3	5.4±1.4	<0.001*,d,f,g,j, 0.009c, 0.002h
Calcium, mg/dl	9.6±0.7	9.5±0.4	9.3±0.5	9.3±0.5	9.0±1.0	0.008*, 0.041d, 0.009g
CaxP, mg²/dl²	35.9±6.4	34.5±7.5	35.4±7.6	45.2±12.7	47.6±12.6	<0.001*,g,j, 0.033c, 0.001d,f, 0.002h
Parathomon, pq/ml	49.5(12-131)	83.05(22.6-722)	147.2(10.2-414)	305.5(74.5-1167)	337(49.3-1426)	<0.001*,c,d,f,g,j, 0.005h
25 OH D vitamin, ng/ml	13.3±10.4	19.6±10.4	18.6±13	15.3±8.0	12.0±10.3	0.010*, 0.014g, 0.046j
HbA1C, (%)	7.3±2.2	6.7±1.5	6.2±1.5	6.3±1.7	5.7±0.9	0.001*, 0.002d, 0.018g
CRP, mg/dl	0.6 (0.31-3.11)	0.5(0.1-2.5)	0.5(0.12-6.2)	0.5(0.16-7.8)	0.7(0.18-9.8)	0.074*
T. Cholesterol, mg/dl	193±41	191±44	183±48	189±47	193±50	0.885*
LDL, mg/dl	115±36	118±38	111±36	117±36	119±47	0.889*
HDL, mg/dl	37±7	37±8	35±7	41±13	37±11	0.349*
Triglyceride, mg/dl	221±104	180±85	175±103	154±95	187±139	0.407*
LVMI, gr/m2	92.1±15.3	94.6±24.2	105.3±19.9	110.9±27.6	106.8±32.2	0.035*
LVH, yes(%)/no	3(17.6)/14	12(31.6)/26	22(56.4)/17	14(60.9)/9	22(48.9)/33	0.014*

SBP: systolic blood pressure, DBP: Diastolic blood pressure, BP: Blood pressure, HT: Hypertension, CCB: Calcium channel blocker, ACEI: Angiotensin-converting enzyme inhibitor, ARB: Angiotensin receptor blocker, CKD: Chronic kidney disease, GFR: Glomerular filtration rate, DM: Diabetes mellitus, LVMI: Left ventricular mass index

*All group, astage2-3, bstage2-4, cstage2-5ND, dstage2-5D, estage3-4, fstage3-5ND, gstage3-5D, hstage4-5ND, istage 4-5D, kstage5-5D

Table 2. Comparing patients with/without left ventricular hypertrophy in chronic kidney patients (n=162)

Parameters	LVH, yes (n=73)	LVH, no (n=89)	p
Male/Female (n/n)	46/27	54/35	0.444
Age, year	53.7±13.1	50.8±14.2	0.174
eGFR, ml/min/1.73m^2	21.4±16.6	30.3±23.2	**0.007**
BMI, kg/m2	26.4±4.4	27.6±4.1	0.081
SBP, mmHg	138±18.4	130±17.5	**0.006**
DBP, mmHg	83.4±9.9	80±10.8	**0.043**
ACEI,n(%)	12 (16.4)	18(20.2)	0.341
ARB,n(%)	12(16.4)	16(18)	0.482
CCB, n(%)	35(47.9)	39(43.8)	0.357
Beta blocker, n(%)	35(47.9)	23(25.8)	0.003
Diuretic, n(%)	24(32.9)	27(30.3)	0.429
CKD time, month	39.3±32.3	38.8±38.1	0.939
Smokers, yes (%)	39(53.4)	47(52.8)	0.264
DM, n(%)	30(41.1)	28(31.5)	0.134
FGF23, pg/ml	9.6(3-189.7)	9(3.3-179.3)	0.439
Hgb, g/dl	11.4±2.05	11.9±1.9	0.085
Ferritin, ng/ml	95.5(9-977)	75(6-1075)	0.812
Glucose, mg/dl	118±55.8	117.6±59.8	0.968
BUN, mg/dl	47.4±25.8	37.9±21.2	**0.011**
Creatinine,mg/dl	4.6±3.2	4±3.5	0.237
Albumin, g/dl	3.5±0.5	3.7±0.6	**0.009**
Calcium, mg/dl	9.2±0.7	9.3±0.7	0.871
PTH, pg/ml	199(10.2-870.3)	147.2(12-1426)	0.668
25 OH D vitamin, ng/ml	14.5±9.1	17.2±12.4	0.125
HbA1C, %	6.4±1.5	6.2±1.5	0.488
CRP, mg/dl	0.6(0.1-9.8)	0.5(0.1-7.82)	0.538
T. Cholesterol, mg/dl	190±52	190±42	0.988
LDL, mg/dl	118±42	114±38	0.507
HDL, mg/dl	36.8±9.4	37.6±9.6	0.602
Triglyceride, mg/dl	168.3±86.5	192.3±125.5	0.167

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BP: Blood pressure, CCB: Calcium channel blocker, ACEI: Angiotensin-converting enzyme inhibitor, ARB: Angiotensin receptor blocker, CKD: Chronic kidney disease, GFR: Glomerular filtration rate, DM: Diabetes mellitus, LVH: left ventricular hypertrophy

Table 3. Echocardiographical parameters according to stages of chronic kidney disease (n:162).

Variables	Stage 2 (n=17)	Stage 3 (n=38)	Stage 4 (n=39)	Stage 5ND (n=23)	Stage 5D (n=45)	P value
LVMI, gr/m^2	92.1±15.3	94.6±24.2	105.3±19.9	110.9±27.5	106.8±32.2	[*]0.035
EF, %	61.1±3.3	62.7±4.2	63±4.5	62.8±4.9	60.6 ±6.9	0.167
LVEDD, mm	44.9±3.6	46.5±4.7	48.4±4.4	48.7±4.9	48.5±4.6	[*]0.019 , [d]0.049
LVESD, mm	29.1±3.9	29.2±3.4	30.7±4.1	30.2±3.5	30.7±4.8	0.314
PWT, mm	10.7±0.96	10.2±1.23	10.8±1.37	10.8±1.35	10.4±1.4	0.221
IVST, mm	11.2±1.44	11.3±1.59	11.5±1.52	11.4±1.8	11.1±1.8	0.836
LAD, mm	34.5±5.15	36.9±5.12	37±4.65	35.7±5.3	37.5±3.9	0.279

LVM: Left ventricular mass, LVMI: Left ventricular mass index, EF: Ejection fraction, LVEDD: Left ventricular end-diastolic diameter, LVESD: Left ventricular end-systolic diameter, PWT: Posterior wall thickness, IVST: Interventricular septum thickness, LAD: Sol atrium diameter

*All group, astage2-3, bstage2-4, cstage2-5ND, dstage2-5D, estage3-4, fstage3-5ND, gstage3-5D, hstage4-5ND, stage 4-5D

Table 4. Multinomial logistic regression analysis of the relationship between clinical characteristics and left ventricular geometry

	Concentric remodeling			Concentric LVH			Eccentric LVH		
	β	OR (95%CI)	p	β	OR (95%CI)	p	β	OR (95%CI)	p
Age	-1.983	0.138(0.027-0.697)	0.017	-1.081	0.339(0.54-2.116)	0.247	-1.983	0.138(0.019-0.983)	0.048
GFR	1.354	3.873(1.172-12.797)	0.026	-0.236	0.790(0.212-2.942)	0.725	0.306	1.357(0.256-7.198)	0.720
SBP	0.365	1.440(0.559-3.714)	0.450	-0.365	0.694(0.259-1.863)	0.469	-0.355	0.701(0.206-2.389)	0.570
Hgb	0.683	1.980(0.491-7.981)	0.337	-0.119	0.888(0.232-3.392)	0.862	0.013	1.013(0.186-5.532)	0.988
Albumin	-0.940	0.391(0.145-1.054)	0.063	-1.473	0.229(0.073-0.719)	0.012	-2.261	0.104(0.18-0.595)	0.011
FGF23	-1.056	0.348(0.086-1.401)	0.137	-1.297	0.273(0.063-1.191)	0.084	-0.351	0.704(0.090-5.529)	0.738
P	-0.026	0.975(0.246-3.853)	0.971	0.316	1.371(0.330-5.699)	0.664	-0.974	0.378(0.055-2.606)	0.323
CaxP	0.205	1.227(0.199-7.577)	0.826	0.278	1.320(0.232-7.501)	0.754	-0.311	0.733(0.049-11.067)	0.822
PTH	0.222	1.249(0.392-3.977)	0.707	-0.091	0.913(0.270-3.085)	0.884	0.177	1.194(0.254-5.616)	0.823
HbA1C	0.318	1.374(0.519-3.639)	0.522	1.505	4.504(1.579-12.844)	0.005	0.015	1.015(0.264-3.901)	0.982
LDL	0.147	0.815(0.312-2.129)	0.676	0.851	2.343(0.729-7.532)	0.153	0.855	2.350(0.563-9.814)	0.241
CRP	0.248	1.282(0.464-3.539)	0.632	-0.414	0.661(0.221-1.980)	0.460	0.659	1.933(0.552-6.774)	0.303
Na	0.717	2.049(0.807-5.204)	0.132	1.415	4.118(1.371-12.368)	0.012	-0.083	0.920(0.268-3.162)	0.895

Age<65 years, SBP (systolic blood pressure) <140/90 mmHg, Hgb <10 g/dl, Albumin <4 g/dl, eGFR <30 ml/min/1.73m², Sodium (Na) <135 mmol/l, CRP<0.8 mg/dl, Phosphorus (P) <5 mg/dl, Parathormon (PTH) <150 pg/ml, LDL<100 mg/dl, HbA1C < 6%

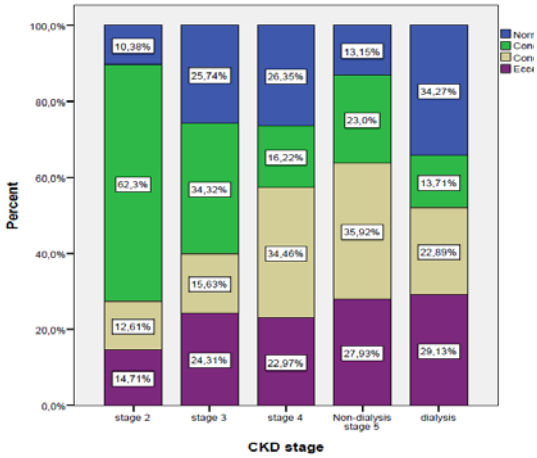

Figure 1. Left ventricular geometry according to the stage of chronic kidney disease patients (n=162)

LVCR started in the early CKD stages (62.3% in stage 2), and its frequency was lower in the advanced stages (13.71% in 5D). The frequency of cLVH progressively increased as the CKD stage increased, and was most common in 5ND (35.92%). The frequency of eLVH was highest in the advanced stages, and especially in 5D (29.13%). Comparing patients with/without LVH serum albumin(p=0.009), GFR (p=0.007), systolic BP (p=0.006), diastolic BP (p=0.043) and BUN (p=0.011) were found different (Table 2).

According to the echocardiographic parameters, LVMI was found to increase as the CKD stage increased, and was found to be lower in 5D than in 5ND (Table 3). The affecting factors were age (β=-1.983, p=0.017) and GFR (β=1.354, p=0.026) for LVCR, and HbA1C (β=1.505, p=0.005), serum albumin (β=-1.473, p=0.012), and serum sodium (β=1.415, p=0.012) for cLVH, and age (β=-1.983, p=0.048) and serum albumin (β=-2.261, p=0.011) for eLVH (Table 4).

DISCUSSION

The close link between kidney and heart disease has been known for a long time. The decrease in GFR is associated with volume retention and increased preload in the heart. Hemodynamic load increases muscle contraction with neurohumoral mechanisms, and over time, cardiac hypertrophy develops[22]. Changes in the cardiovascular system develop in the early stages of CKD lead to an increase in morbidity and mortality. LVH, one of these cardiovascular complications, is an independent risk factor for

myocardial infarct, heart failure, arrhythmia, and other cardiovascular deaths[23,24]. However, multiple randomized clinical trials were showed that intensive HD reduces cardiac hypertrophy[25-28]. The prevalence of LVH found to be 43.6 and 48.9 percent in predialysis and dialysis patients in our study, respectively, and was lower than the reported in the literature (51.2%, 53%) and (54.6%)[29-31]. The younger age of the CKD patients (5D patients, 47.9±15.2 years) in our study might have played a role in this discrepancy.

In our patients older than 65 years, eLVH and LVCR were more common. Physiological cardiac changes caused by aging, additionally progressive AS and cardiac effects, can lead to the left ventricle more sensitive to volume and pressure load. LV dilatation is an independent predictor for mortality in ESRD patients[32]. eLVH, the echocardiographic finding of left ventricular dilation, was detected in our 5D group at most. Dialysis patients are likely at risk for eccentric LVH because they are under an overload due to anuria or inadequate dialysis.

In our study, LVH saw in the early stages of CKD and increased as the CKD stage increased. It was most common in stage 5ND, and less in stage 5D than stage 5ND patients. It suggests that cardiac changes occur at a very early stage. Dialysis in CKD-5D can effectively treat as uremia, hypervolemia, acidosis, hyperphosphatemia, and anemia. The higher detection of LVH in stage 5D compared to 5ND may result from the left ventricle exposed to pressure and volume load in the predialysis-stage. On the other hand, in stage 5D, cardiac hypertrophy may be resolved as a result of the resolution of many complications through dialysis treatment. However, some such patients may have died due to cardiovascular problems or for other reasons before reaching the dialysis stage.

Interestingly, the prevalence of patients with LVNG was higher than the rate of LVNG (17.7%) reported by Nube et all[33] (17.7%) and the highest in 5D (34.27%). The presence of LVNG patients in a substantial ratio, even among patients with 5D, suggests that cardiac disorders in CKD may be preventable. However, early CKD patients with LVH may not reach the 5D period. The cross-sectional nature of our study is insufficient to explain this high rate.

In CKD stage 2, LVCR was the most common, and LVNG was the least. As reported to Park et all[34], substantial changes in the cardiovascular system started in our study from the early CKD stage. Unlike LVCR, the frequency of cLVH increased as the CKD stage progressed and was highest in the 5ND group. These findings may be attributed to calcium-phosphorus metabolism disorders, inflammation, and uremic toxins related to the CKD progression and co-morbid diseases such as HTN and DM. Considering that many CKD complications are preventable through the dialysis treatment, the lower rate of cLVH in the 5D group compared to the 5ND suggests that the cardiovascular complications of CKD may partially improve with dialysis treatment.

Nube et all[33] reported that eLVH (44%) is the most common type of LVG in dialysis patients. In our study, eLVH (29.13%) was highest but lower in 5D patients. In stage 5ND, the most frequently detected cLVH was associated with low serum Na and albumin and high HbA1c. Nutritional disorders and fluid and electrolyte imbalances, which commonly seen in the CKD 5ND group, may explain these findings. On the other hand, younger age and decreased albumin levels were found to be significant in eLVH compared to LVNG. Serum albumin is a negative inflammatory marker, and the presence of inflammation together with hypoalbuminemia is associated with endothelial dysfunction, atherosclerosis, and cardiovascular mortality in CKD patients[35]. Hypoalbuminemia may also be a marker of malnutrition or hypervolemia. However, since serum CRP levels were found to be low in our patients, this may be primarily associated with hypervolemia. Both hypervolemia and malnutrition may play a role in the development of CVD[36-38]. CVD is a significant cause of death in CKD patients, and therefore it is logical to decrease serum albumin with cardiovascular structural changes.

In our study, cLVH was found to be higher among diabetic patients. DM is an important cardiovascular risk factor that causes both macrovascular and microvascular complications. Pathophysiological mechanisms are chronic hyperglycemia, insulin resistance, accumulation of collagen, and glycosylated end products in myocardium[39,40]. Diabetic cardiomyopathy is a condition associated with left ventricular diastolic and systolic dysfunction, cardiomyocyte hypertrophy, myocardial interstitial fibrosis, cardiomyocyte apoptosis, and oxidative stress, and is one of the leading causes of heart failure[40]. The higher rate of detection of cLVH in diabetic patients in our study supports the adverse

outcomes of diabetes on the cardiovascular system.

The LVCR increased in our study with increasing age. Aortic stiffness results in increased systolic BP, decreased diastolic BP, and increased aortic pulse wave velocity and pulse pressure due to reduced elastin and increased collagen with aging[41,42]. Decreased diastolic pressure reduces coronary perfusion, causing myocardial ischemia, and high systolic pressure increases left ventricular load. Chronically high systolic pressure causes an increase in LVH and myocardial oxygen demand in the heart[43]. Many negative factors, such as increased coronary atherosclerosis and impaired myocardial blood flow due to decreased diastolic BP, are responsible for cardiovascular changes in older age.

Serum sodium levels were higher in our cLVH patients than LVNG. cLVH was found at the highest frequency in stage 4 and stage 5, and LVNG in 5D. Dilutional hyponatremia is common in dialysis patients due to hypervolemia. Serum sodium levels were the lowest (134.8 ± 3.2 mmol/l) in 5D compared to other CKD groups. Also, in our study, serum sodium level was found to be lower than 140 mmol/L (mean <136) in all patients who could explain the relationship between cLVH and serum Na.

Interestingly serum FGF 23 levels, which is known as a biomarker for SHPT and cardiovascular disease in CKD patients, did not show any correlation or difference with any echocardiographic parameters. The frequency of LVNG was low in CKD stage 2 and highest in 5D. It may be that early-stage CKD patients are older and cannot reach 5D. Our cross-sectional study cannot explain this situation.

Some limitations of our study include cross-sectional and relatively small sample sizes. Since there may be individual differences in refilling in dialysis patients, there is no consensus about when to monitor cardiac function. However, echocardiography was performed 2-24 hours after dialysis, which is the closest period to the dry weight of the patients.

In conclusion, we can say that abnormal LVG at CKD, which is an indicator of the risk of cardiovascular disease, started in the early stages. The higher risk of cardiovascular disease in advanced stages may be related to the higher incidence of eLVH and cLVH. Nontraditional factors such as volume status and nutrition may also be related to left ventricular remodeling.

Yazar Katkıları: Çalışma konsepti/Tasarımı: BK; Veri toplama: İK, NS, BK; Veri analizi ve yorumlama: BK, SP; Yazı taslağı: BK; İçeriğin eleştirel incelenmesi: BK, SP; Son onay ve sorumluluk: BK, SP, NS, MB, İK; Teknik ve malzeme desteği: NS; Süpervizyon: SP; Fon sağlama (mevcut ise): yok.
Etik Onay: Bu çalışma için Çukurova Üniversitesi Tıp Fakültesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulundan 05.01.2012 tarih ve 4/4 kararı ile etik onay alınmıştır.
Hakem Değerlendirmesi: Dış bağımsız.
Çıkar Çatışması: Yazarlar çıkar çatışması beyan etmemişlerdir.
Finansal Destek: Yazarlar finansal destek beyan etmemişlerdir.

Author Contributions: Concept/Design : BK; Data acquisition: İK, NS, BK; Data analysis and interpretation: BK, SP; Drafting manuscript: BK; Critical revision of manuscript: BK, SP; Final approval and accountability: BK, SP, NS, MB, İK; Technical or material support: NS; Supervision: SP; Securing funding (if available): n/a.
Ethical Approval: For this study, ethics approval was obtained from Çukurova University Faculty of Medicine non-interventional clinical research Ethics Committee on 05.01.2012 with decision 4/4.
Peer-review: Externally peer-reviewed.
Conflict of Interest: Authors declared no conflict of interest.
Financial Disclosure: Authors declared no financial support

REFERENCES

1. Foley RN, Parfrey PS, Sarnak MJ. Epidemiology of cardiovascular disease in chronic renal disease. J Am Soc Nephrol. 1998;9:16-23.
2. Shlipak MG, Fried LF, Cushman M, Manolio TA, Peterson D, Stehman-Breen C et al. Cardiovascular mortality risk in chronic kidney disease: comparison of traditional and novel risk factors. JAMA. 2005;293:1737-45.
3. National Cholesterol Education Program Expert Panel on Detection E, Treatment of High Blood Cholesterol in A. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002;106:3143-421.
4. Ravarotto V, Simioni F, Pagnin E, Davis PA, Calo LA. Oxidative stress - chronic kidney disease - cardiovascular disease: A vicious circle. Life Sci. 2018;210:125-31.
5. Ardahanli I, Celik M. Can myocardial performance index predict early cardiac risks in erectile dysfunction? Aging Male 2020; doi: 10.1080/13685538.2020.1768367:1-7.
6. London GM. Cardiovascular disease in chronic renal failure: pathophysiologic aspects. Semin Dial. 2003;16:85-94.
7. Zoccali C, Benedetto FA, Mallamaci F, Tripepi G, Giacone G, Stancanelli B et al. Left ventricular mass monitoring in the follow-up of dialysis patients: prognostic value of left ventricular hypertrophy progression. Kidney Int. 2004;65:1492-8.
8. Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. N Engl J Med. 1990;322:1561-6.

9. Park CW, Shin YS, Kim CM, Lee SY, Yu SE, Kim SY et al. Increased C-reactive protein following hemodialysis predicts cardiac hypertrophy in chronic hemodialysis patients. Am J Kidney Dis. 2002;40:1230-9.
10. Chirakarnjanakorn S, Navaneethan SD, Francis GS, Tang WH. Cardiovascular impact in patients undergoing maintenance hemodialysis: Clinical management considerations. Int J Cardiol. 2017;232:12-23.
11. Paoletti E, Bellino D, Cassottana P, Rolla D, Cannella G. Left ventricular hypertrophy in nondiabetic predialysis CKD. Am J Kidney Dis. 2005;46:320-7.
12. Malyala R, Rapi L, Nash MM, Prasad GVR. Pre-transplant left ventricular geometry and major adverse cardiovascular events after kidney transplantation. Ann Transplant. 2019;24:100-7.
13. 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, a branch of the European Society of Cardiology. J Am Soc Echocardiogr. 2005;18:1440-63.
14. Park M, Hsu CY, Li Y, Mishra RK, Keane M, Rosas SE, et al. Associations between kidney function and subclinical cardiac abnormalities in CKD. J Am Soc Nephrol. 2012;23:1725-34.
15. Bansal N, Keane M, Delafontaine P, Dries D, Foster E, Gadegbeku CA et al. A longitudinal study of left ventricular function and structure from CKD to ESRD: the CRIC study. Clin J Am Soc Nephrol. 2013;8:355-62.
16. de Roij van Zuijdewijn CL, Hansildaar R, Bots ML, Blankestijn PJ, van den Dorpel MA, Grooteman MP et al. Eccentric left ventricular hypertrophy and sudden death in patients with end-stage kidney disease. Am J Nephrol. 2015;42:126-33.
17. Lieb W, Gona P, Larson MG, Aragam J, Zile MR, Cheng S et al. The natural history of left ventricular geometry in the community: clinical correlates and prognostic significance of change in LV geometric pattern. JACC Cardiovasc Imaging. 2014;7:870-8.
18. Eckardt KU, Scherhag A, Macdougall IC, Tsakiris D, Clyne N, Locatelli F et al. Left ventricular geometry predicts cardiovascular outcomes associated with anemia correction in CKD. J Am Soc Nephrol. 2009;20:2651-60.
19. Paoletti E, De Nicola L, Gabbai FB, Chiodini P, Ravera M, Pieracci L et al. Associations of left ventricular hypertrophy and geometry with adverse outcomes in patients with CKD and hypertension. Clin J Am Soc Nephrol 2016; 11:271-9.
20. National Kidney F. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002;39:1-266.
21. Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I et al. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. Am J Cardiol 1986;57:450-8.
22. Lorell BH, Carabello BA. Left ventricular hypertrophy: pathogenesis, detection, and prognosis. Circulation 2000; 102:470-9.
23. Chen SC, Huang JC, Tsai YC, Chen LI, Su HM, Chang JM et al. Body Mass Index, Left Ventricular Mass Index and Cardiovascular Events in Chronic Kidney Disease. Am J Med Sci. 2016;351:91-6.
24. 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.
25. McCullough PA, Chan CT, Weinhandl ED, Burkart JM, Bakris GL. Intensive hemodialysis, left ventricular hypertrophy, and cardiovascular disease. Am J Kidney Dis. 2016;68:5-14.
26. Chan CT, Floras JS, Miller JA, Richardson RM, Pierratos A. Regression of left ventricular hypertrophy after conversion to nocturnal hemodialysis. Kidney Int. 2002;61:2235-9.
27. Ayus JC, Mizani MR, Achinger SG, Thadhani R, Go AS, Lee S. Effects of short daily versus conventional hemodialysis on left ventricular hypertrophy and inflammatory markers: a prospective, controlled study. J Am Soc Nephrol. 2005;16:2778-88.
28. Rocco MV, Lockridge RS, Jr., Beck GJ, Eggers PW, Gassman JJ, Greene T et al. The effects of frequent nocturnal home hemodialysis: the Frequent Hemodialysis Network Nocturnal Trial. Kidney Int. 2011;80:1080-91.
29. Vigan J, Ahoui S, Hounsou D, Goudote ACK, Vehounkpe Sacca J. Left ventricular hypertrophy in chronic hemodialysis patients at CNHU-HKM of Cotonou. Nephrol Ther. 2018; 14:29-34.
30. Bregman R, Lemos C, Pecoits Filho R, Abensur H, Draibe S, Bastos MG et al. Left ventricular hypertrophy in patients with chronic kidney disease under conservative treatment. J Bras Nefrol. 2010;32:83-8.
31. Dobre M, Roy J, Tao K, Anderson AH, Bansal N, Chen J et al. Serum bicarbonate and structural and functional cardiac abnormalities in chronic kidney disease - a report from the Chronic Renal Insufficiency Cohort Study. Am J Nephrol. 2016;43:411-20.
32. Foley RN, Parfrey PS, Harnett JD, Kent GM, Murray DC, Barre PE. The prognostic importance of left ventricular geometry in uremic cardiomyopathy. J Am Soc Nephrol. 1995;5:2024-31.
33. Nube MJ, Hoekstra T, Doganer V, Bots ML, Blankestijn PJ, van den Dorpel M et al. Left ventricular geometric patterns in end-stage kidney

disease: Determinants and course over time. Hemodial Int 2018; doi: 10.1111/hdi.12644.
34. Park SK, Jung JY, Kang JG, Chung PW, Ryoo JH. Mildly decreased renal function and its relation to left ventricular geometry change. Circ J. 2019;83:2236-41.
35. Alves FC, Sun J, Qureshi AR, Dai L, Snaedal S, Barany P et al. The higher mortality associated with low serum albumin is dependent on systemic inflammation in end-stage kidney disease. PLoS One. 2018;13:e0190410.
36. Perunicic-Pekovic G, Rasic-Milutinovic Z, Pljesa S. [Predictors of mortality in dialysis patients--association between malnutrition, inflammation and atherosclerosis (MIA syndrome)]. Med Pregl. 2004;57:149-52.
37. 7. Stenvinkel P, Heimburger O, Paultre F, Diczfalusy U, Wang T, Berglund L et al. Strong association between malnutrition, inflammation, and atherosclerosis in chronic renal failure. Kidney Int. 1999;55:1899-911.
38. Agarwal R. Hypervolemia is associated with increased mortality among hemodialysis patients. Hypertension. 2010;56:512-7.
39. Petrie JR, Guzik TJ, Touyz RM. Diabetes, hypertension, and cardiovascular disease: clinical insights and vascular mechanisms. Can J Cardiol. 2018;34:575-84.
40. Glezeva N, Chisale M, McDonald K, Ledwidge M, Gallagher J, Watson CJ. Diabetes and complications of the heart in Sub-Saharan Africa: An urgent need for improved awareness, diagnostics and management. Diabetes Res Clin Pract. 2018;137:10-9.
41. Zieman SJ, Melenovsky V, Kass DA. Mechanisms, pathophysiology, and therapy of arterial stiffness. Arterioscler Thromb Vasc Biol. 2005;25:932-43.
42. McEniery CM, Wilkinson IB, Avolio AP. Age, hypertension and arterial function. Clin Exp Pharmacol Physiol. 2007;34:665-71.
43. Paneni F, Diaz Canestro C, Libby P, Luscher TF, Camici GG. The aging cardiovascular system: understanding it at the cellular and clinical levels. J Am Coll Cardiol. 2017;69:1952-67.