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NEPHROLOGY - ORIGINAL PAPER

Echocardiographic predictors of interatrial block in patients with severe chronic kidney disease

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Abstract

Background Interatrial block (IAB), defined as a conduction delay between the right and left atrium, is manifested on the electrocardiogram as a prolonged P-wave duration. Large number of studies recently have been published regarding the prevalence of IAB and its associations with the risk of atrial fibrillation and ischemic stroke. Cardiovascular diseases are the leading causes of mortality in chronic kidney disease (CKD). In this study, we aimed to investigate echocardiographic predictors of IAB in patients with severe CKD.

Methods This study enrolled a total of 155 patients [male: 95 (61.3%), mean age: 56.3 ± 12.8 years] with severe CKD (glomerular filtration rate < 30 mL/min). All patients were evaluated by electrocardiography and transthoracic echocardiography. IAB was defined as P wave duration of ≥ 120 ms on electrocardiography.

Results Electrocardiography revealed IAB in 54 patients. The baseline demographic characteristics of the patients were similar in both groups with and without IAB. Left atrial diameter (LAD), left ventricular end-systolic and end-diastolic diameters, interventricular septal thickness, posterior wall thickness, left ventricular mass, left ventricular mass index (LVMI), and the prevalence of left ventricular hypertrophy were found to be significantly increased in patients with IAB. Increased LAD (OR = 1.119; 95% CI 1.019–1.228; $p = 0.019$) and LVMI (OR = 1.036; 95% CI 1.003–1.070; $p = 0.031$) were found to be independent predictors of IAB.

Conclusion A significant association exists between the presence of IAB and echocardiographic parameters related to left ventricular hypertrophy and left atrial dilatation. Presence of IAB may be an additional and easy diagnostic marker for risk stratification of patients with severe CKD.

Keywords Chronic kidney disease · Echocardiography · Electrocardiography · Interatrial block

Introduction

Cardiovascular complications have been reported to be the main cause of mortality in patients with chronic kidney disease (CKD) [1]. The pathogenesis of cardiovascular complications in these patients is complex and multifactorial including vascular changes, degeneration of cardiomyocytes, left ventricle hypertrophy, and arrhythmia as well as traditional risk factors such as hypertension, dyslipidemia, and diabetes mellitus [2–4]. The most common clinical presentation of cardiac impairments in the course of CKD is probably the left ventricle hypertrophy [1]. However, it should be noted that in patients with CKD cardiovascular complications may also include disturbances of the conduction system. Electrolyte disturbance including hypocalcemia can lead to disturbed transmission of electrical impulses in cardiomyocytes [2]. These conduction problems in the uremic heart may lead to delayed atrial and ventricular depolarization and subsequently prolonged *P* wave and QRS complex durations on surface electrocardiography (ECG).

Interatrial block (IAB) is defined as a delayed or blocked electrical conduction between the right and left atrium

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and is manifested as a *P* wave duration of ≥ 120 ms on the surface ECG [5]. The interest in this topic has increased in recent years, and a large number of studies have been recently published regarding the prevalence of IAB and its associations with ischemic stroke and supraventricular arrhythmias including atrial fibrillation [6–10]. Atrial dilatation and fibrosis are considered as the major contributors to the underlying pathophysiological mechanisms of IAB through altering the structural and electrical properties of cardiac myocytes [11, 12]. Left ventricular hypertrophy, myocardial ischemia, and conduction system disturbances have been reported to be common cardiovascular complications in patients with CKD [13, 14]. Previously, increased *P* wave duration and IAB were reported in patients with CKD as compared to healthy controls [15]. However, echocardiographic predictors of IAB in CKD patients have not been investigated yet.

In this study, we hypothesized that the presence of IAB may be related with echocardiographic parameters in patients with CKD. Thus, we aimed to investigate echocardiographic predictors of IAB in patients with severe CKD.

Methods

Study population

This single-center study enrolled a total of 155 patients (male: 95, mean age: 56.3 ± 12.8 years) with severe CKD (glomerular filtration rate < 30 mL/min). Patients who were diagnosed with coronary artery disease, history of myocardial infarction, left ventricular dysfunction (left ventricular ejection fraction < 50%), moderate to severe heart valve disease, cardiomyopathy, arrhythmia, high degree atrioventricular block, complete bundle branch block, active infection, connective tissue disease and liver or thyroid dysfunction were excluded from the study. All patients underwent transthoracic echocardiography (TTE) and 12-lead high-resolution surface ECG. The study population was divided into two groups according the presence of IAB on ECG. All demographic, electrocardiographic, and echocardiographic parameters were recorded into a dataset and compared between CKD patients with and without IAB. All patients provided a written informed consent and the study protocol was approved by the local ethics committee of the hospital in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

Echocardiography

All patients underwent TTE performed by two experienced cardiologists using Vivid 5 echocardiography device (GE Vingmed Ultrasound AS, Horten, Norway), and 3.2 mHz adult probe with the patient in the left lateral decubitus position. In all patients, left atrial diameter (LAD), interventricular septal thickness (IVST), posterior wall thickness (PWT), left ventricular end-systolic (LVESD), and end-diastolic diameters (LVEDD) were measured on the parasternal long-axis view. Left ventricular ejection fractions (LVEF) of the patients were calculated using biplane Simpson's method. Left ventricular mass (LVM) was calculated based on Devereux formula [$LVM = 0.8\ (1.04\ (IVST + LVEDD + PWT)^3 - (LVEDD)^3) + 0.6$], and body surface area was estimated using Mosteller formula [$\text{body surface area} = (\text{height (cm)} \times \text{body weight (kg)}/3600)^{1/2}$]. Left ventricular mass was divided by body surface area to estimate left ventricular mass index (LVMI).

Electrocardiographic analysis

A 12-lead high-resolution ECG, which was recorded at a speed of 25 mm/s and a voltage of 10 mm/mV, was obtained from all patients after a 10-min rest (Nihon Kohden Cardiofax ECG-9132). Patients were allowed to breathe freely but not to speak or cough during recordings. All ECG papers were scanned, loaded to a computer, magnified sufficiently, and analyzed with a digital image processing software (imagej. nih.gov/ij/). Measurements were calibrated on the underlying standard ECG graph paper. All measurements were calculated by two independent cardiologists blinded to other patients' clinical information. The onset and the end of the P-waves were marked with the cursor on a high-resolution computer screen to calculate P-wave duration in all leads. The beginning of the P wave was defined as the point where the initial deflection of the P wave crossed the isoelectric line, and the end of the P wave was defined as the point where the final deflection of the P wave crossed the isoelectric line. Presence of IAB was defined as P wave duration of ≥ 120 ms on ECG. P wave dispersion was defined as the difference between the widest and the narrowest P wave duration recorded from the 12 ECG leads. The PR interval was defined as the period that extends from the beginning of the P wave until the beginning of the QRS complex. The QRS duration was defined as the interval from the start of the QRS complex until J point. QT interval was defined as the interval from the onset of the QRS complex to the end of the T wave. The R-R interval was measured and used to compute the heart rate and to correct QT interval (QTc) with the Bazett's Formula. ($QTc = QT/\sqrt{\text{R-R interval in seconds}}$). All durations were calculated in milliseconds and the mean values were calculated from 12 ECG leads. In patients on hemodialysis, ECG was recorded just before a midweek hemodialysis.

Laboratory analysis

To perform complete blood count and blood chemistry panel, venous blood samples were collected after 12-h of fasting by a clean puncture of an antecubital vein from all patients. Complete blood countings were measured on Sysmex XT2000i analyzer (Sysmex Corporation, Kobe, Japan). Fasting blood glucose, blood urea nitrogen, creatinine, sodium, potassium, calcium, phosphorus, uric acid, total protein, alanine aminotransferase, aspartate aminotransferase, total cholesterol (TC), high-density lipoprotein (HDL), and triglyceride (TG) levels were also measured on an autoanalyzer (Siemens Advia 2400 Chemistry System, Siemens Diagnostic, Tarrytown, USA). Low-density lipoprotein (LDL), was calculated using the Friedewald formula [LDL (mg/dL) = TC − (HDL + TG/5)] [16]. The glomerular filtration rate was calculated as a function of age, serum creatinine, and race using the simplified modified diet in renal disease (MDRD) equation [17].

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 19.0. (IBM Corp. Armonk, NY). Descriptive statistics were reported as mean ± standard deviation for continuous variables with normal distribution or median (25th–75th percentiles) values for continuous variables without normal distribution and as frequency with percentages for the categorical variables. The Shapiro–Wilk and Kolmogorov–Smirnov tests were used to test the normality of the distribution of continuous variables. Categorical variables were compared with chi-square or Fisher exact tests. Student *t* test or Mann–Whitney *U* test was used to compare continuous variables as appropriate. The significance level was accepted as $p < 0.05$ in all statistical analyses. A logistic regression analysis was performed to identify any independent echocardiographic associates of IAB. A receiver operating characteristic (ROC) curve analysis was performed to evaluate the sensitivity, specificity, area under the curve (AUC), and confidence interval (CI) of parameters for predicting IAB. Bland Altman analysis (MedCalc software for Windows) was used to compare ROC curve analysis results for LAD and LVMI. Intra and inter observer agreement was assessed using Cohen's kappa test. The mean inter and intra observer agreement was 91% and 94% respectively.

Results

The ECG revealed IAB in 54 patients and the study population was divided into two groups as patients with IAB (mean age: 57.7 ± 14.1 years, male: 36) and patients without IAB (mean age: 55.6 ± 12.1 years, male: 59). Comparison of the clinical, demographical, and laboratory characteristics between CKD patients with and without IAB was presented in Table 1. Age and gender distribution were similar between groups. There was also no significant difference in terms of body mass index, systolic and diastolic blood pressures, glomerular filtration rate, the frequencies of diabetes mellitus, hypertension, dyslipidemia, smoking, hemodialysis status, and beta blocker usage (Table 1).

Upon comparison of laboratory parameters between CKD patients with and without IAB, there was no significant difference in terms of routine serum biomarkers such as fasting blood glucose, blood urea nitrogen, creatinine, sodium, potassium, calcium, phosphorus, uric acid, total protein, alanine aminotransferase, aspartate aminotransferase, total cholesterol, HDL, LDL, triglyceride, and complete blood count parameters including white blood cells, hemoglobin, and platelets (Table 1).

Comparison of the echocardiographic and electrocardiographic parameters between CKD patients with and without IAB was presented in Table 2. Among echocardiographic parameters, only LVEF (59.8 ± 4.9 vs 61.9 ± 5.8%, $p = 0.025$) was significantly lower in patients with IAB. All other echocardiographic parameters including LVESD (32.7 ± 4.7 vs 30.2 ± 5.9 mm, $p = 0.007$), LVEDD (47.3 ± 5.1 vs 44.8 ± 6.2 mm, $p = 0.014$), LAD (39.8 ± 5.1 vs 35.8 ± 4.4 mm, $p < 0.001$) (Fig. 1a), IVST (12.3 ± 1.6 vs 11.1 ± 1.9 mm, $p < 0.001$), PWT (12.4 ± 1.8 vs 10.8 ± 1.9 mm, $p < 0.001$), LVM (213.2 ± 65.1 vs 167.6 ± 62.4 g, $p < 0.001$), LVMI (118.3 ± 33.1 vs 90.4 ± 33.7 g/m^2, $p < 0.001$) (Fig. 2a) and the prevalence of LVH (53.7 vs 32.7%, $p = 0.011$) were significantly higher in patients with IAB (Table 2).

Comparison of electrocardiographic parameters yielded that there was no significant difference in terms of heart rate (79.9 ± 12.1 vs 80.1 ± 13.4 bpm, $p = 0.599$), PR interval (217.1 ± 78.3 vs 203.4 ± 84.2 ms, $p = 0.327$), QRS duration (96.5 ± 18.1 vs 91.5 ± 18.9 ms, $p = 0.116$), QT interval (380.2 ± 56.7 vs 383.7 ± 35.9 ms, $p = 0.635$) and calculated QTc (432.2 ± 31.5 vs 426.6 ± 53.7 ms, $p = 0.484$) between the groups. However, P wave duration (132.4 ± 13.2 vs 109.7 ± 8.1 ms, $p < 0.001$) and P wave dispersion (21.1 ± 11.4 vs 15.6 ± 6.5 ms, $p = 0.002$) were significantly higher in patients with IAB (Table 2). Since hemodialysis may effect electrocardiographic parameters via factors such as volume overload, rapid changes in electrolytes, patients were divided into two groups as "hemodialysis patients" and "non-hemodialysis patients". All comparisons were repeated in these separate groups and the results were presented in Table 2.

The univariate associates of IAB were taken into multiple logistic regression analysis. Increased LAD (OR = 1.119; 95% CI 1.019–1.228; $p = 0.019$) and LVMI (OR = 1.036; 95% CI 1.003–1.070; $p = 0.031$) were identified as

Table 1 Comparison of the clinical, demographic, and laboratory characteristics of the patients with and without interatrial block

Variables	IAB (+) (*n*: 54)	IAB (−) (*n*: 101)	*p* value
Baseline demographics parameters			
Age, years	57.7 ± 14.1	55.6 ± 12.1	0.344
Gender, male (*n*, %)	36 (66.7)	59 (58.4)	0.315
Hypertension (*n*, %)	37 (68.5)	65 (64.4)	0.603
Diabetes mellitus (*n*, %)	14 (25.9)	22 (21.8)	0.561
Dyslipidemia (*n*, %)	11 (20.4)	14 (13.9)	0.294
Smoking (*n*, %)	7 (13)	17 (17)	0.510
Hemodialysis (*n*, %)	29 (53.7)	45 (44.6)	0.277
Glomerular filtration rate (ml/dk/1.73 m^2)	14.2 ± 7.2	15.1 ± 7.5	0.453
Body mass index (kg/m^2)	26.7 ± 3.1	27.8 ± 4.9	0.161
Systolic blood pressure (mmHg)	130.7 ± 17.7	128.6 ± 18.2	0.493
Diastolic blood pressure (mmHg)	82.5 ± 12.4	82.4 ± 11.8	0.994
Beta blocker usage (*n*, %)	22 (40.7)	52 (51.4)	0.202
Laboratory parameters			
WBC (×10^3/mL)	6.8 ± 1.8	6.6 ± 1.7	0.390
Hemoglobin (g/dL)	13.4 ± 1.9	13.2 ± 2.1	0.621
Platelet (×10^3cells/dL)	229 ± 52	237 ± 63	0.443
Glucose (mg/dL)	119.5 ± 43.8	109.7 ± 36.1	0.138
BUN (mg/dL)	61.5 ± 15.4	60.4 ± 16.8	0.702
Creatinine (mg/dL)	5.6 ± 2.1	5.3 ± 2.4	0.524
Calcium (mg/dL)	9.1 ± 0.8	9.2 ± 0.7	0.361
Phosphorus (mg/dL)	4.0 ± 1.1	3.9 ± 1.3	0.656
Total protein (g/dL)	7.2 ± 0.6	7.3 ± 0.5	0.826
Uric acid (mg/dL)	4.9 ± 1.2	4.8 ± 1.4	0.413
Aspartate aminotransferase (U/L)	19 (14–23)	20 (16–24)	0.305
Alanine aminotransferase (U/L)	15 (10–23)	17 (14–25)	0.160
Sodium (mEq/L)	138.1 ± 2.8	138.7 ± 2.2	0.128
Potassium (mEq/L)	4.7 ± 0.6	4.6 ± 0.6	0.557
Total cholesterol (mg/dL)	191.7 ± 49.6	190.7 ± 45.6	0.908
Triglyceride (mg/dL)	191.7 ± 41.4	173.6 ± 55.1	0.451
Low-density lipoprotein (mg/dL)	114.6 ± 40.4	115.4 ± 35.7	0.905
High-density lipoprotein (mg/dL)	39.8 ± 9.3	41.4 ± 13.4	0.127

BUN blood urea nitrogen, *IAB* interatrial block, *WBC* white blood cell [continuous variables with normal distribution were expressed as mean ± standard deviation and continuous variables without normal distribution were expressed as median (25th–75th percentiles)]

independent predictors of IAB (Table 3). Among hemodialysis patients, multiple logistic regression analysis could not determine an independent predictor for IAB (Table 4). Whereas, in non-hemodialysis patient group, LAD (OR = 1.324; 95% CI 1.012–1.742; $p = 0.011$) and LVMI (OR = 1.110; 95% CI 1.035–1.191; $p = 0.003$) were again identified as independent predictors of IAB (Table 5).

In the ROC curve analysis, LAD higher than 35 mm predicted the presence of IAB with a sensitivity of 75% and a specificity of 65% (AUC: 0.750; 95% CI 0.669–0.831; $p < 0.001$) (Fig. 1b), LVMI higher than 104.5 g/m^2 predicted the presence of IAB with a sensitivity of 74% and a specificity of 72% (AUC: 0.741; 95% CI 0.662–0.819; $p < 0.001$) (Fig. 2b). When compared with Bland–Altman analysis, there was no significant difference between the AUCs of ROC curves for LAD and LVMI ($z = 1.32$; $p = 0.146$) (Fig. 3).

Correlation analyses were performed between electrocardiographic and echocardiographic parameters. There was a significant and moderate positive correlation between P wave duration and LAD ($r = 0.567$, $p < 0.001$) (Fig. 4a) and also a significant and moderate positive correlation between P wave duration and LVMI ($r = 0.517$, $p < 0.001$) (Fig. 4b).

Discussion

In this case–control study, we have focused on the relationship between the presence of IAB and echocardiographic parameters in patients with severe CKD. Echocardiographic

Table 2 Comparison of the echocardiographic and electrocardiographic parameters of the patients with and without interatrial block

Variables	All patients			HD patients			Non-HD patients		
	IAB (+) (*n*: 54)	IAB (−) (*n*: 101)	*p* value	IAB (+) (*n*: 29)	IAB (−) (*n*: 45)	*p* value	IAB (+) (*n*: 25)	IAB (−) (*n*: 56)	*p* value
Echocardiography parameters									
LV ejection fraction (%)	59.8 ± 4.9	61.9 ± 5.8	0.025	59.0 ± 6.1	60.6 ± 7.1	0.299	60.8 ± 3.2	63.0 ± 4.5	0.030
Left atrial diameter (mm)	39.8 ± 5.1	35.8 ± 4.4	< 0.001	37.4 ± 4.8	35.3 ± 5.1	0.068	36.2 ± 5.3	32.3 ± 3.4	< 0.001
LV end-diastolic diameter (mm)	47.3 ± 5.1	44.8 ± 6.2	0.014	47.9 ± 5.6	47.4 ± 6.4	0.711	46.4 ± 4.1	42.7 ± 5.2	0.002
LV end-systolic diameter (mm)	32.7 ± 4.7	30.2 ± 5.9	0.007	32.8 ± 5.1	31.2 ± 6.3	0.231	32.6 ± 4.4	29.4 ± 5.5	0.011
Interventricular septal thickness (mm)	12.3 ± 1.6	11.1 ± 1.9	< 0.001	12.7 ± 1.7	11.8 ± 2.1	0.068	12.0 ± 1.6	10.4 ± 1.7	< 0.001
Posterior wall thickness (mm)	12.4 ± 1.8	10.8 ± 1.9	< 0.001	12.5 ± 1.6	11.7 ± 2.1	0.063	12.2 ± 2.1	10.2 ± 1.6	< 0.001
LV mass, (g)	213.2 ± 65.1	167.6 ± 62.4	< 0.001	237.7 ± 69.4	192.2 ± 68.1	0.007	184.7 ± 46.5	147.8 ± 49.9	0.002
LV mass index, (g/m^2)	118.3 ± 33.1	90.4 ± 33.7	< 0.001	130.3 ± 36.9	104.9 ± 39.3	0.006	104.3 ± 20.8	78.7 ± 23.1	< 0.001
LV hypertrophy, *n* (%)	29 (53.7)	33 (32.7)	0.011	19 (65.5)	23 (51.1)	0.222	10 (40)	10 (17.9)	0.033
Electrocardiography parameters									
Heart rate (bpm)	79.9 ± 12.1	80.1 ± 13.4	0.599	78.7 ± 15.9	79.2 ± 12.3	0.867	72.8 ± 11.7	75.1 ± 9.7	0.378
P wave duration (ms)	132.4 ± 13.2	109.7 ± 8.1	< 0.001	131.3 ± 12.1	109.2 ± 7.3	< 0.001	133.9 ± 14.5	110.3 ± 8.6	< 0.001
P wave dispersion (msec)	21.1 ± 11.4	15.6 ± 6.5	0.002	20.7 ± 13.4	15.4 ± 6.8	0.028	21.5 ± 8.9	15.7 ± 6.3	0.003
PR interval (msec)	217.1 ± 78.3	203.4 ± 84.2	0.327	220.4 ± 83.1	199.7 ± 91.1	0.327	213.4 ± 73.9	206.6 ± 78.8	0.718
QRS duration (msec)	96.5 ± 18.1	91.5 ± 18.9	0.116	93.3 ± 17.1	94.7 ± 16.2	0.725	100.2 ± 18.9	88.8 ± 20.7	0.023
QT interval (msec)	380.2 ± 56.7	383.7 ± 35.9	0.635	382.9 ± 29.1	382.6 ± 41.7	0.965	376.9 ± 78.1	384.7 ± 30.8	0.526
Corrected QT interval (msec)	432.2 ± 31.5	426.6 ± 53.7	0.484	435.9 ± 33.5	437.0 ± 44.9	0.916	427.8 ± 29.1	417.9 ± 59.2	0.432

BUN blood urea nitrogen, *IAB* interatrial block, *HD* hemodialysis, *LV* left ventricle, *WBC* white blood cell [continuous variables with normal distribution were expressed as mean ± standard deviation and continuous variables without normal distribution were expressed as median (25th–75th percentiles)]

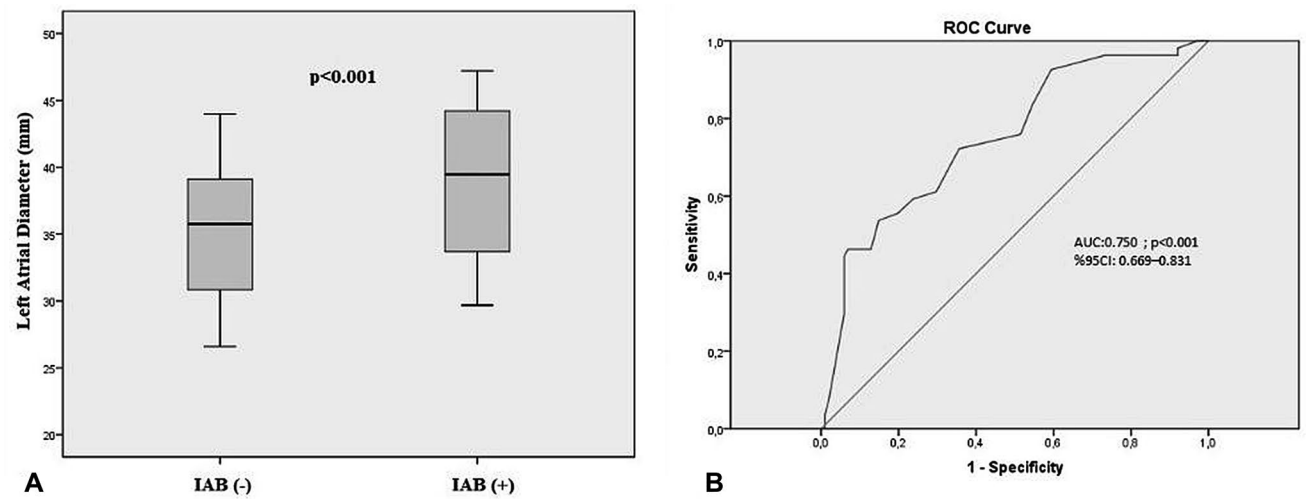

Fig. 1 The box-plot graph comparing the left atrial diameters between patients with and without IAB (**a**). Receiver operating characteristic curve revealing the AUC for left atrial diameter to predict the presence of IAB (*AUC* area under the curve, *CI* confidence interval, *IAB* interatrial block)

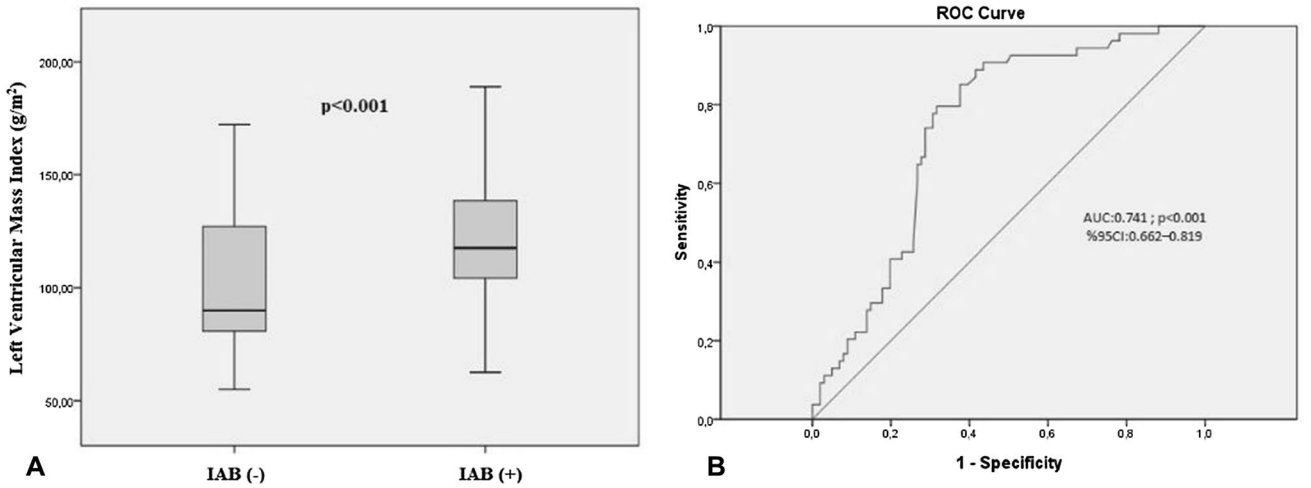

Fig. 2 The box-plot graph comparing the left ventricular mass index values between patients with and without IAB (**a**). Receiver operating characteristic curve revealing the AUC for left ventricular mass index to predict the presence of IAB (*AUC* area under the curve, *CI* confidence interval, *IAB* interatrial block)

Table 3 Multivariate regression analysis showing independent predictors of interatrial block

	OR	95% CI	*p* value
Left ventricular ejection fraction	0.983	0.912–1.060	0.657
Left atrial diameter	1.119	1.019–1.228	0.019
Left ventricular end systolic diameter	1.036	0.939–1.143	0.477
Left ventricular end diastolic diameter	0.977	0.877–1.089	0.674
Interventricular septal thickness	0.731	0.328–1.629	0.444
Posterior wall thickness	1.769	0.825–3.792	0.143
Left ventricular mass	0.988	0.970–1.006	0.198
Left ventricular mass index	1.036	1.003–1.070	0.031
Left ventricular hypertrophy	1.359	0.448–4.124	0.589

CI confidence interval; *OR* odds ratio

Table 4 Multivariate regression analysis results in hemodialysis patients

	OR	95% CI	*p* value
Left atrial diameter	1.035	0.926–1.158	0.543
Interventricular septal thickness	1.078	0.450–2.582	0.867
Posterior wall thickness	0.963	0.382–2.426	0.936
Left ventricular mass	1.004	0.984–1.023	0.719
Left ventricular mass index	1.008	0.977–1.041	0.605

CI confidence interval; *OR* odds ratio

parameters related to left ventricular hypertrophy and left atrial dilatation have been found to be significantly increased in CKD patients with IAB. Furthermore, increased LAD and LVMI were identified as independent predictors of IAB in these patients.

Table 5 Multivariate regression analysis results in non-hemodialysis patients

	OR	95% CI	*p* value
Left ventricular ejection fraction	0.988	0.832–1.173	0.888
Left atrial diameter	1.324	1.012–1.742	0.011
Left ventricular end systolic diameter	0.984	0.808–1.197	0.869
Left ventricular end diastolic diameter	1.134	0.908–1.417	0.268
Interventricular septal thickness	0.762	0.146–3.987	0.747
Posterior wall thickness	2,946	0.657–13.206	0.158
Left ventricular mass	0.939	0.902–1.008	0.133
Left ventricular mass index	1.110	1.035–1.191	0.003
Left ventricular hypertrophy	0,379	0.040–3.595	0.398

CI confidence interval; *OR* odds ratio

The incidence of cardiovascular diseases and deaths from cardiovascular events have been reported to be increased in CKD patients as compared to the general population [18]. It was reported previously that, majority of adult patients have cardiovascular diseases diagnosed at the time of CKD onset, and approximately half of deaths are attributed to cardiovascular events [19]. In addition to the traditional risk factors such as hypertension, dyslipidemia, and diabetes mellitus, non-traditional risk factors such as anemia [20], overhydration [21], endothelial dysfunction [22], hypocalcemia [23] and hyperparathyroidism [24] have been accused in the pathophysiological mechanisms of cardiovascular complications in these patients.

Left ventricular hypertrophy is a common pathology in patients with CKD. Cardiac hypertrophy is a response of the myocardium to increased workload. Initial cardiac

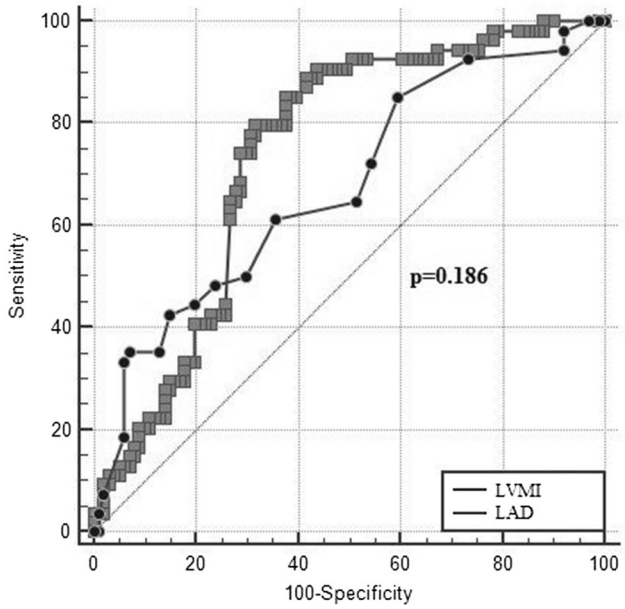

Fig. 3 Comparison of receiver operating characteristic curves of left atrial diameter and left ventricular mass index for predicting the presence of interatrial block

hypertrophy constitutes an adaptive mechanism, but prolonged and severe hypertrophy is a risk factor for arrhythmias, sudden death, and heart failure [25]. CKD patients with left ventricular hypertrophy have an increased risk of cardiovascular events and, specifically, an increased risk of sudden cardiac death [26–28]. There is also evidence for that concentric remodeling of the left ventricle may increase cardiovascular risk [29]. Increased accumulation of collagen due to left ventricular hypertrophy may result in myocardial fibrosis and decreased cardiac reserve. Thus, cardiac conduction disorders may occur [30].

ECG is a simple, non-invasive, and readily available tool in daily routine practice. IAB, which is a newly introduced ECG parameter, is defined as the prolongation of the conduction time between the right and left atrium due to an impulse delay or blockage most often in the Bachmann's bundle. Several previous studies reported that IAB is related with the development of new-onset atrial fibrillation in patients with coronary artery disease and peripheral vascular disease [31, 32]. Moreover, a significant relationship has been reported between the presence of IAB and ischemic stroke [9, 10]. In a previous study, high prevalence of IAB was reported in patients with end-stage renal disease [15]. However, echocardiographic determinants of IAB have never been investigated in these patients.

In this study, presence of IAB has been associated with increased LVMI which is an objective measure of left ventricular hypertrophy. Left ventricular hypertrophy may cause a decrease in left ventricular compliance with increased left ventricular end-diastolic pressure and left atrial pressure, thus, may increase the duration of the P wave in patients with CKD [33]. Since left ventricular hypertrophy has been associated with increased morbidity and mortality in these patients, presence of IAB on surface ECG may be an additional and easy diagnostic tool for risk stratification of patients with CKD. Those with IAB may be particularly at risk for cardiovascular complications. ECG is a cheap and easy assessable diagnostic tool and can be also interpreted

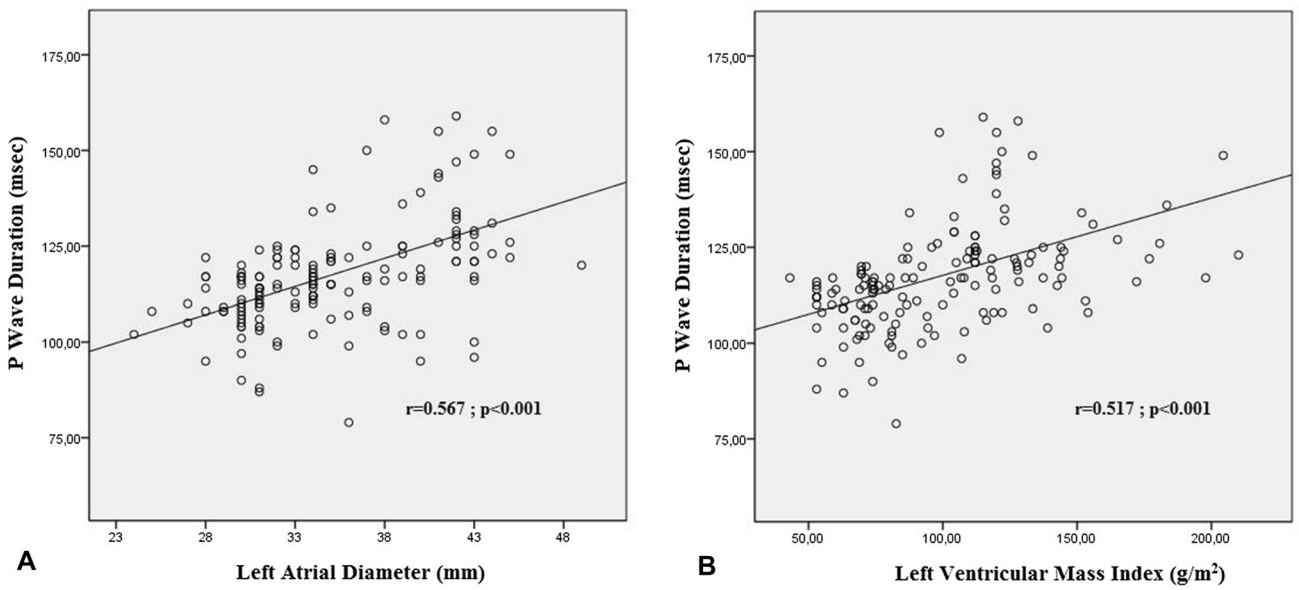

Fig. 4 The scatter plot graphs revealing the moderate positive correlation between P wave duration and left atrial diameter (**a**), and also between P wave duration and left ventricular mass index (**b**)

by nephrologists. Since the presence of IAB has been associated with increased LVMI which is a well-known marker of cardiovascular risk, the nephrologists may refer the patient to the cardiologists for echocardiographic evaluation when they detected IAB on ECG.

The presence of IAB has been also associated with increased LAD in the present study. Volume overload and coronary artery disease causing ischemia may be etiological factors for left atrial dilatation in patients with CKD. Myocardial ischemia may cause a decrease in left ventricular compliance, resulting in an increase in left ventricular end-diastolic pressure and left atrial pressure. The increase in left atrial pressure leads to an increase in left atrial size. The increase in the size of the left atrium also prolongs the P wave duration [34]. During atrial remodeling, atrial dilatation, and fibrosis alters the structural and electrical properties of cardiac myocytes and may be considered as the major contributors to the underlying pathophysiological mechanisms of IAB [11, 12].

Secondary hyperparathyroidism is an inevitable component of CKD and serves as a significant causative factor for both structural changes in the heart and conduction problems in transmitting electrical impulses [35]. Serum calcium–phosphate imbalance in patients with CKD may affect the metabolism of individual tissues and cells. Considerable intracellular calcium ion accumulation in various organs may lead to different clinical dysfunctions in the course of CKD [36]. It is commonly accepted that hypocalcemia can lead to defective muscle contractions and disturbed transmission of electrical impulses in cardiomyocytes [37]. The reason for that conduction failure is probably related to the fact that calcium depletion compromises the membrane calcium channel activity and the inward flow of calcium ions to cardiomyocytes, which is necessary for action potential and proper depolarization progress in the heart [38]. The above-mentioned calcium-phosphate metabolism disorders could be considered as the pathomechanisms underlying the presence of IAB in patients with CKD. However, there was no significant difference in terms of electrolyte levels between CKD patients with and without IAB in our study. Furthermore, many patients, especially those who are more vulnerable to cardiovascular diseases such as the elderly and the diabetics, frequently suffer from adynamic bone disease [39].

Study limitations

The primary limitation was that our study was a nonrandomized and single-center study with a relatively small number of patients. Unfortunately, the design of this case–control study was not prospective and therefore lacks data regarding the follow up of the patients. Also, pre-study ECG characteristics of the study population were unknown.

Conclusion

The present study demonstrated that there was a significant relationship between the presence of IAB and echocardiographic parameters related to left ventricular hypertrophy and left atrial dilatation in patients with severe CKD. Especially, increased LAD and LVMI were strongly associated with the presence of IAB in these patients. Since left ventricular hypertrophy has been associated with increased morbidity and mortality, the presence of IAB may be an additional and easy diagnostic marker for risk stratification of patients with severe CKD. Those with IAB on ECG may be particularly at risk for cardiovascular complications.

Author contributions All of the authors contributed planning, conduct, and reporting of the work. All authors had full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Compliance with ethical standards

Conflict of interest All of the authors have no conflict of interest.

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