ORIGINAL ARTICLE

Ventricular ECG Abnormalities as a Predictor of Mortality Outcomes in Non-Dialysis Chronic Kidney Disease Patients

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Background: About half of the mortality of patients with chronic kidney disease (CKD) was attributable to cardiovascular causes, as evidenced by cardiac structural remodeling that could be detected on a surface electrocardiogram (ECG). However, the ability of ECG abnormalities to predict survival outcomes in CKD patients remained inconclusive.

Objective: To identify the ventricular ECG abnormalities that could predict long-term mortality in non-dialysis CKD patients with cardiovascular risks.

Materials and Methods: The authors conducted an analysis of data from the CORE-CKD (Thailand) registry, which included pre-dialysis CKD patients with cardiovascular risks. Baseline demographic data and co-morbidities were recorded. All baseline ECG were reviewed to determine the pertinent ventricular ECG abnormalities, including three voltage criteria for ventricular hypertrophy (Cornell, Sokolow-Lyon, and Peguro-Lo Presti criteria), QRS duration, bundle branch block, left anterior and posterior fascicular block, QT interval, QRS and T wave angle, QRS-T angle, poor R wave progression in chest leads, and pathological Q wave. Cox regression analysis was utilized to estimate the prognostic value of all relevant ECG parameters for survival.

Results: The baseline 12-lead ECG and complete long-term outcome data were available for 251 patients. Median age was 66, with an IQR of 59 to 70 years. Median eGFR was 36.35 (27.78 to 46.43) mL/minute/1.73 m^2 with diabetic nephropathy accounting for the majority of cases. Thirteen patients (5.1%) died during the median follow-up of 58.4 (29.0 to 61.1) months. After Cox regression analysis adjusted with potential confounding factors including age and gender, Cornell's criteria for left ventricular hypertrophy (LVH) (adjusted HR 7.94, 95% CI 1.58 to 39.85, p=0.012) and left posterior fascicular block (LPFB) (adjusted HR 11.33, 95% CI 1.40 to 91.32, p=0.039) were associated with increased risk of all-cause mortality.

Conclusion: LVH by Cornell voltage criteria and LPFB were associated with an increased risk of all-cause mortality in pre-dialysis CKD patients with cardiovascular risks.

Keywords: Chronic kidney disease; Electrocardiogram; Left posterior fascicular block; Left ventricular hypertrophy; Cornell voltage criteria

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Cardiovascular diseases in chronic kidney disease (CKD) patients are the most probably caused by a systemic proinflammatory condition, leading to the development of atherosclerotic plaques, abnormal calcification, and myocardial fibrosis[1]. As a result, about 40% to 50% of all fatalities in individuals with moderate to severe CKD are due to cardiovascular causes, compared to 26% of the normal kidney function group. The leading causes of cardiovascular mortality are primarily due to myocardial infarction, cardiac arrhythmias, and heart failure, all of which are complicated by structural remodeling[2]. Several treatment approaches for cardiovascular diseases are limited and may be ineffective in advanced stages of CKD. Consequently, the development of simplified predictive tools could be beneficial for early optimization of cardiovascular risk factors and improving outcomes for CKD patients.

In the context of detecting structural remodeling, a surface 12-lead electrocardiography (ECG) is a non-invasive, cost-effective, and widely used technology that is accessible in various healthcare settings. It is recommended for the initial evaluation of all CKD patients in accordance with the standard guidelines[3]. Patients with CKD exhibited a significantly higher incidence of abnormal baseline ECG than the

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general population, particularly left ventricular (LV) abnormalities such as LV hypertrophy (LVH), atrioventricular block, inter and intraventricular conduction abnormalities, pathological Q wave, abnormal ventricular repolarization such as ST segment deviation, T wave abnormalities, and QT prolongation[4,5]. These findings have been correlated to the cardiovascular outcomes and death of patients with CKD in multiple studies[4-6]. However, most of these research had focused on non-Asian patients with advanced CKD, including those undergoing hemodialysis. Therefore, the authors aimed to determine ventricular ECG abnormalities as a predictor of long-term all-cause mortality in non-dialysis CKD patients in Thailand.

Materials and Methods

Design and setting

The data utilized in the present study were sourced from the CORE-CKD Thailand cohort, which was a prospective, multicenter, hospital-based, non-interventional cohort that included CKD patients with a high risk of cardiovascular events or renal disease progression. The present cohort was approved by the Central Research Ethics Committee (CREC: COA-CRE 004/2014) of the Faculty of Medicine Chiang Mai University (approval No.161/2022). The registry enrolled patients between August 2014 and March 2019. Patients with CKD stages 3 to 5 at a significant risk of cardiovascular events or renal progression were included in the study. CKD stages were defined by estimated glomerular filtration rate (eGFR) from Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation[7].

Study population

The analysis comprised patients aged 18 years or older and had a baseline 12-lead ECG that could be interpreted. Patients with a ventricular paced rhythm at the beginning of the study were excluded. Baseline demographic and clinical information, such as age, gender, body mass index, smoking, etiologies of CKD, presence of diabetes mellitus, hypertension, dyslipidemia, coronary artery disease, atrial fibrillation/flutter, cerebrovascular accidents such as transient ischemic attack or stroke, chronic heart failure, chronic lung disease, chronic liver disease, and malignancy, were obtained. Medications currently in use, and initial laboratory test results, were documented

ECG interpretations and measurements and definitions

During the registration process, 12-lead ECG were obtained while the participant was at rest. A licensed cardiologist reviewed and evaluated the ECGs to detect any ventricular abnormalities. The determined abnormalities encompassed LVH, right ventricular hypertrophy (RVH), frontal QRS axis, frontal QRS-T angle, QRS duration (QRSd), bundle branch and fascicular block, pathologic Q wave, precordial R wave progression, and QT interval with corrected QT interval (QTc).

The existence of LVH was determined by achieving one of the aforementioned criteria: either one of the Cornell voltage combination criteria as the sum of R in aVL and SV3 equal or greater than 20 mm in females or equal or greater than 28 mm in males[8], or Sokolow-Lyon criteria, which is the sum of R in V5/6 and SV1 equal or greater than 35 mm[9], or Peguero-Lo Presti criteria, which is the sum of deepest S and S in V4 that is greater than 23 in females or greater than 28 in males[10]. RVH was determined based on the fulfillment of one of the following criteria: Tall R in V1 greater than 6 mm, Deep S in V5 greater than 10 mm or Deep S in V6 greater than 3 mm, RV1 + S V5,6 greater than 10.5 mm, R:S ratio V1 greater than 1[9,11]. QRSd was measured from the beginning to the offset of QRS complex at the J point, which is the end of QRS complex to ST junction.

The presence of either preexisting complete right bundle branch block (RBBB), left bundle branch block (LBBB), left anterior fascicular block (LAFB), or left posterior fascicular block (LPFB) was determined based on specific criteria outlined in the consensus[12]. The possibility of any type of conduction aberrancy was ruled out, and these conditions were interpreted as intrinsic QRS complex without effect of conduction aberrancy.

The measurement of the QT interval was performed by measuring the time from the onset of QRS complex to the end of T wave, which was determined using the tangent method[13]. The QTc with the preceding RR interval was calculated using the Bazett's formula[14]. In the presence of bundle branch block, the simplified formula QTc = measured QT interval – 0.5 × measured QRS interval, was used[15].

The QRS frontal axis, QRS-T angle, and QRSd were gathered from the measurement of the ECG machine. Pathologic Q wave were following the universal definition[16].

To obtain accurate values, the authors utilized

EP Calipers software (version 3.8.0, © 2015-2023 EP Studios, Inc.) for calibration and precise measurements, with two licensed cardiologists with proven low intra- and interobserver variations.

Vital status monitoring

Patients in the cohort were evaluated at the center every four to six months up to five years. If they were unable to follow up, a telephone call was used to confirm vital status. The vital status of all patients was confirmed using the national database of vital statistics.

Sample size estimation

According to the study conducted by Agarwal & Light[17], the adjusted hazard ratio (HR) for all-cause death in patients with ECG-LVH, as determined by the Sokolow-Lyon criteria, was 2.84. A minimum of 244 patients were necessary to establish the distinction in cardiovascular outcomes in electrocardiographic LVH with 80% statistical power.

Statistical analysis

Variables were represented and analyzed based on their specific characteristics. Categorical variables were presented as frequency, percentage and compared by using chi-square test. Continuous variables with normal distribution were presented as mean ± standard deviation (SD) and compared by using independent t-test. The non-normally distributed data were presented as median, interquartile range, and p-value, and were compared between groups using the Mann-Whitney U test. The binary logistic regression approach was used to conduct both univariable and multivariable analysis. The Kaplan-Meier method was employed to do survival analysis. In the multivariable analysis, variables that had a p-value of less than 0.1 from the univariate analysis, as well as pre-determined risk factors such as age, gender, and eGFR, were included in the multivariable logistic regression.

Statistical significance was indicated by a p-value of less than 0.05. The statistical analyses were conducted using IBM SPSS Statistics, version 23.0 (IBM Corp., Armonk, NY, USA).

Results

Baseline characteristics

A baseline 12-lead ECG was recorded on 517 patients in the registry. The final analysis included 251 patients (48.5%) who had complete long-term follow-up data (Figure 1). Table 1 presented the

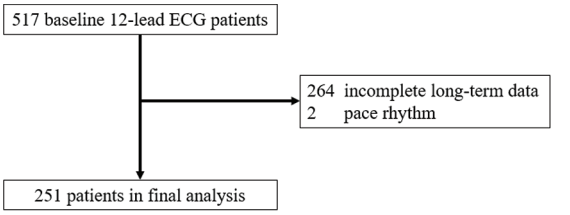

Figure 1. Flow diagram of patient selection.

baseline characteristics and comparison between survivors and non-survivors. The median age of the patients included in the present study was 66 years (IQR 59 to 70), and 153 (61.0%) of them were male. The most prevalent comorbidity was hypertension in 88.8%, followed by dyslipidemia in 70.9%, and type 2 diabetes mellitus in 48.2%. A majority of patients were classified in CKD stage 3, thus 68.1%. The median eGFR was 36.35 (27.8 to 46.4) mL/minute/1.73 m². The most common cause of CKD among the present study population was diabetic nephropathy in 45.8%, followed by hypertensive nephropathy in 32.3%.

Thirteen patients (5.1%) died during the median follow-up of 58.4 (29.0 to 61.1) months. Most baseline characteristics were not different between survivor and non-survivor groups except higher total cholesterol level in the non-survivor group. Both groups exhibited comparable baseline medications, with the exception of a greater prevalence of statin usage among survivors as illustrated in Table 1.

ECG findings

Table 2 showed ECG findings and comparison between survivors and non-survivors. The baseline ECG of the included patients was predominantly in sinus rhythm. Among the 251 patients, 43 patients (17.1%) exhibited LVH as determined by any voltage criteria. The majority of these cases (76.7%), which is 33 out of 43 patients, were identified using the Peguero-Lo Presti's criteria. LVH determined by overall voltage criteria was found to be higher in CKD stage 4 to 5 compared to lower stages of CKD at 25.0% versus 14.0% (p=0.036). The prevalence of LVH was similar between hypertensive patients and non-hypertensive patients at 17.0% versus 17.9% (p=0.914). No difference in LVH diagnosis based on any criterion was seen between survivors and non-survivors.

Out of 251 patients, only 12 (4.8%) had a QRSd greater than 120 ms, and most of these patients were diagnosed with RBBB. Notably, none of the patients with a QRSd above 120 ms were among the

Table 1. Baseline characteristics of survivals and non-survivors (n=251)

Characteristics	Survivors (n=238)	Non-survivors (n=13)	p-value
Age (years); median (IQR)	65.00 (59.00, 70.00)	69.00 (60.00, 73.00)	0.170
Male; n (%)	144 (60.5)	9 (69.2)	0.771
Cause of CKD; n (%)			
Diabetic nephropathy	109 (45.8)	6 (46.2)	0.980
Hypertensive nephropathy	77 (32.4)	4 (30.8)	1.00
Glomerulonephritis	13 (5.5)	0 (0)	1.000
Renal stone disease	14 (5.9)	1 (7.7)	0.560
Comorbidities; n (%)			
Type 2 DM	114 (47.9)	7 (53.8)	0.676
Hypertension	211 (88.7)	12 (92.3)	1.000
Dyslipidemia	170 (71.4)	8 (61.5)	0.531
Malignancy	16 (6.7)	0 (0)	1.000
Atrial fibrillation	11 (4.6)	0 (0)	1.000
Coronary artery disease	0 (0.0)	1 (7.7)	0.052
Chronic heart failure	4 (1.7)	0 (0)	1.000
Ischemic stroke	9 (3.8)	1 (7.7)	0.418
History of smoking	80 (33.6)	8 (61.5)	0.069
Body weight (kg); median (IQR)	66.95 (60.00, 76.13)	71.00 (55.50, 81.45)	0.934
Serum creatinine (mg/dL); median (IQR)	1.77 (1.48, 2.22)	1.80 (1.58, 2.85)	0.365
eGFR (mL/min/1.73 m^2); median (IQR)	36.30 (28.00, 46.43)	39.55 (22.48, 47.53)	0.600
CKD stage; n (%)			
CKD stage 2 or lower	7 (2.9)	0 (0.0)	1.000
CKD stage 3	164 (68.9)	7 (53.8)	0.256
CKD stage 4	66 (27.7)	5 (38.5)	0.527
CKD stage 5	1 (0.4)	0 (0.0)	1.000
UPCI; median (IQR)	0.34 (0.10, 1.15)	1.03 (0.12, 2.41)	0.256
Total cholesterol level (mg/dL); median (IQR)	173.00 (150.00, 196.00)	205.00 (188.00, 218.00)	0.017
Triglycerides (mg/dL); median (IQR)	122.00 (91.00, 171.00)	145.00 (91.00, 250.00)	0.308
HDL-C (mg/dL); median (IQR)	47.50 (39.00, 56.00)	49.00 (40.50, 59.00)	0.693
LDL-C (mg/dL); median (IQR)	94.00 (78.00, 118.50)	123.00 (102.50, 142.50)	0.020
Baseline medications; n (%)			
Antiplatelets	92 (38.7)	4 (30.8)	0.771
Oral anticoagulants	10 (4.2)	0 (0.0)	1.000
Beta blocker	77 (32.4)	7 (53.8)	0.110
ACEi	44 (18.5)	2 (15.4)	1.000
ARB	86 (36.1)	2 (15.4)	0.148
Diuretic	64 (26.9)	2 (15.4)	0.523
Spironolactone	9 (3.8)	0 (0.0)	1.000
Statin	174 (73.1)	6 (46.2)	0.036

ACEi=angiotensin-converting enzyme inhibitors; ARB=angiotensin receptor blockers; CKD=chronic kidney disease; DM=diabetes mellitus; eGFR=estimated glomerular filtration rate; HDL-C=high-density lipoprotein cholesterol; IQR=interquartile range; LDL-C=low-density lipoprotein cholesterol; UPCI=urine protein to creatinine index

non-survivors.

The median QTc, frontal QRS, and T and QRS-T axis were within the normal range, and there was no significant difference between the survivors and non-survivors. The present study population exhibited a low prevalence of pathological Q waves and poor R progression.

Survival outcomes

During the median follow-up period of 58.4 (29.0 to 61.1) months, 13 patients (5.1%) died with median time to death of 33.0 months (range 11.1 to 54.7). Univariable analysis with baseline variables and interested ECG findings are shown in Table 3. The univariable analysis identified the presence of LVH

Table 2. ECG findings of survivors and non-survivors

ECG findings	Survivors (n=238)	Non-survivors (n=13)	p-value
Sinus rhythm; n (%)	231 (97.1)	12 (92.3)	0.351
Atrial fibrillation; n (%)	7 (2.9)	1 (7.7)	0.351
LVH by ECG criteria; n (%)	39 (16.4)	4 (30.8)	0.246
LVH by Cornell's	10 (4.2)	2 (15.4)	0.122
LVH by Sokolow-Lyon's	12 (5.0)	1 (7.7)	0.508
LVH by Peguero-Lo Presti's	31 (13.0)	2 (15.4)	0.683
RVH by ECG criteria; n (%)	15 (6.3)	1 (7.7)	0.584
QRS duration (msec); median (IQR)	92.00 (86.00, 99.25)	84.00 (81.00, 93.50)	0.013
QRS duration >120 msec; n (%)	13 (5.4)	0 (0)	
LBBB; n (%)	1 (0.4)	0 (0.0)	1.000
RBBB; n (%)	8 (3.4)	0 (0.0)	1.000
LAFB; n (%)	4 (1.7)	0 (0.0)	1.000
LPFB; n (%)	3 (1.3)	1 (7.7)	0.193
Corrected QT interval (msec); median (IQR)	427.00 (410.75, 444.00)	425.00 (410.00, 435.00)	0.468
QRS angle (°); median (IQR)	37.00 (10.00, 62.00)	28.00 (–3.50, 57.50)	0.520
T angle (°); median (IQR)	39.00 (23.75, 59.00)	43.00 (34.00, 57.50)	0.458
QRS-T angle (°); median (IQR)	–2.50 (–30.00, 18.25)	–13.00 (–47.50, 6.00)	0.269
PRWP; n (%)	17 (7.1)	1 (7.7)	1.000
Pathologic Q wave; n (%)	11 (4.6)	1 (7.7)	0.480

ECG=electrocardiogram; IQR=interquartile range; LAFB=left anterior fascicular block; LBBB=left bundle branch block; LVH=left ventricular hypertrophy; LPFB=left posterior fascicular block; PRWP=poor R wave progression; RBBB=right bundle branch block; RVH=right ventricular hypertrophy

Table 3. Univariable Cox proportional hazards regression model

Characteristics	Univariable analyses		
	Hazard ratio	95% CI	p-value
Age	1.05	0.972 to 1.137	0.213
Male	0.703	0.216 to 2.283	0.557
Coronary artery disease	21.50	2.72 to 169.87	0.004
Type 2 diabetes	1.36	0.46 to 4.06	0.579
Cerebrovascular disease	4.34	1.19 to 15.78	0.026
History of smoking	3.62	1.18 to 11.08	0.024
eGFR	0.99	0.94 to 1.04	0.737
UPCI	1.18	0.99 to 1.40	0.052
Cholesterol level	1.01	1.00 to 1.03	0.035
LDL-C	1.02	1.00 to 1.03	0.020
LVH by ECG criteria	2.14	0.66 to 6.95	0.205
LVH by Cornell	5.12	1.13 to 23.17	0.034
LVH by Sokolow-Lyon	1.58	0.21 to 12.13	0.663
LVH by Peguro-Lo Presti	1.28	0.28 to 5.77	0.749
RVH	1.39	0.181 to 10.69	0.752
LPFB	8.60	1.11 to 66.46	0.039
Corrected QT interval	0.998	0.979 to 1.017	0.820
QRS-T angle	0.991	0.980 to 1.002	0.117
PRWP	1.22	0.159 to 9.398	0.847
Pathologic Q wave	1.71	0.222 to 13.122	0.608

CI=confidence interval; ECG=electrocardiogram; eGFR=estimated glomerular filtration rate; HR=hazard ratio; LDL-C=low-density lipoprotein cholesterol; LVH=left ventricular hypertrophy; LPFB=left posterior fascicular block; PRWP=poor R wave progression; RVH=right ventricular hypertrophy; UPCI=urine protein to creatinine index

Table 4. Multivariable Cox proportional hazards regression models

	LVH by Cornell's		LPFB	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Model 1	7.94 (1.58 to 39.85)	0.012	11.33 (1.40 to 91.32)	0.039
Model 2	8.40 (1.65 to 42.90)	0.010	15.06 (1.67 to 136.01)	0.016

CI=confidence interval; HR=hazard ratio; LPFB=left posterior fascicular block; LVH=left ventricular hypertrophy

Model 1: adjusted with age and sex; Model 2: adjusted with age, sex, and eGFR

by Cornell voltage criteria and LPFB were linked to a higher risk of all-cause mortality (unadjusted HR 5.12, 95% confidence interval [CI] 1.13 to 23.17, p=0.034 and 8.60, 95% CI 1.11 to 66.46, p=0.039, respectively). The Kaplan-Meier survival curves for the LVH by Cornell voltage criteria and LPFB are presented in Figure 2 and 3.

Despite the significantly higher QRSd in survivors, regression analysis revealed that a QRSd above 120 ms was not significantly associated with mortality (HR 0.047, 95% CI 0.000 to 6,387.704, p=0.611).

Table 4 presents the multivariable regression models adjusted for several potential confounding variables to analyze mortality. Following any model of adjustment, the presence of LVH as determined by Cornell's criteria and LPFB were shown to be

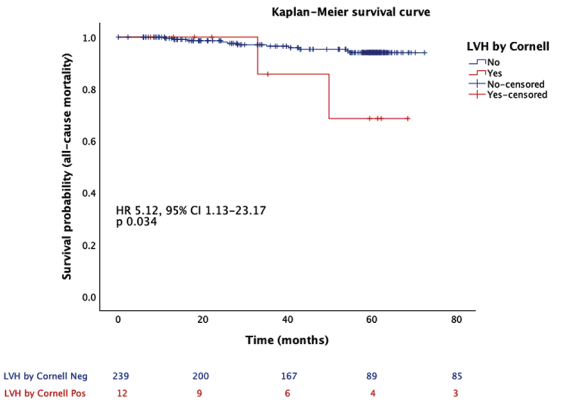

Figure 2. Kaplan-Meier survival curves of unadjusted LVH by Cornell criteria.

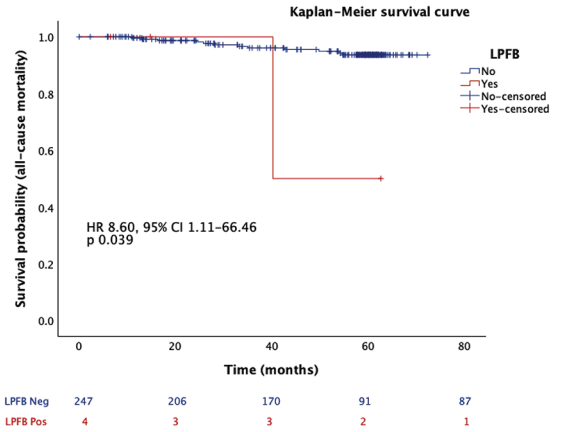

Figure 3. Kaplan-Meier survival curves of unadjusted LPFB.

associated with an elevated mortality rate in the present study population. Additionally, we performed adjustments based on prespecified factors and those with a p-value below 0.1 from the univariate analysis, including coronary artery disease, diabetes mellitus, cerebrovascular accident, smoking history, low-density lipoprotein cholesterol (LDL-C), and QRSd above 120 ms. The results showed that both LVH (according to Cornell's criteria) and LPFB remained independently associated with increased mortality.

The long-term mortality was not associated with the alternative LVH criteria by Sokolow-Lyon and Peguero-Lo Presti in both the unadjusted and adjusted analyses.

Discussion

The present study demonstrated that LVH was the dominating ECG abnormality in individuals with pre-dialysis CKD. This finding was observed in patients both with and without pre-existing hypertension. Previous studies have shown a high prevalence of ECG-LVH in CKD patients, with a range of 7% to 16%[4,17]. The prevalence of LVH in the present study population is comparable to these findings and is higher than that observed in patients with normal renal function. There are numerous factors that elucidate the direct correlation between CKD and LVH. Cardiomyocytes becomes expansion when GFR is lowered, resulting in LVH[18]. Fibroblasts actively enhance the extracellular matrix by releasing collagen precursors and matrix metalloproteinases (MMPs) causing progressive myocardial fibrosis[19]. Various growth factors may have significant roles in cardiac fibrosis in CKD, which results from dysfunctional metabolic and inflammatory processes[20,21]. LVH may be the consequence of hypervolemia-induced elevated preload[21], increased afterload due to elevated peripheral resistance, augmentation of central systolic blood pressure by reflected pressure wave from rigid and calcified blood vessels which commonly found in CKD patients[22]. Additionally, preexisting hypertension, a significant cause of CKD[23], may also contribute to the presence of LVH[23]. Furthermore, other variables that may contribute to the development of LVH include anemia-induced increased cardiac output[24], diabetic cardiomyopathy[25], or autonomic dysregulation[26].

Interestingly, the authors found an association between long-term mortality in non-dialysis CKD patients and the LVH according to Cornell voltage criteria, but not with Sokolow-Lyon criteria or Peguero-Lo Presti criteria. In the previous cohorts, particularly among patients with hypertension, Cornell's LVH criteria had been recognized as an independent predictor of cardiovascular outcomes[27]. Studies conducted on dialytic CKD patients revealed that cardiovascular mortality was associated with both Sokolow-Lyon and Cornell criteria[6,28].

The predictive accuracy of ECG-LVH in pre-dialysis CKD is still a topic of great debate. The present study has provided data on the effectiveness of Cornell voltage criteria in predicting mortality in this population. However, the research conducted by Agarwal & Light, which included 243 pre-dialysis CKD patients, produced results inconsistent with the present study. Their adjusted regression analysis found a correlation between long-term all-cause mortality and ECG-LVH according to the Sokolow-Lyon criteria, but not with the Cornell criteria[17]. The explanation for the disparity between studies remained unclear. Several differences exist between the present study and theirs, including a predominantly

Caucasian population, a higher percentage of patients meeting Sokolow-Lyon criteria in the CKD group at 8% versus 5.2% in the present study, and a higher proportion of established cardiovascular disease, such as coronary artery disease and stroke. This disparity in the cardiac remodeling process among different baselines may be attributed to result variation. Based on ethnic considerations, a report from Asian research indicated that Cornell voltage criteria demonstrated superior sensitivity and diagnostic performance than Sokolow-Lyon criteria in detecting echocardiographic left ventricular hypertrophy within the Asian population[29-31]. The Sokolow-Lyon criteria used exclusively chest leads, which may be more influenced by other factor such as height compared to the Cornell criteria that included the aVL limb lead[31].

The present study was the first to utilize the Peguero-Lo Presti criteria as a definition for ECG-LVH in patients with CKD. Nevertheless, the authors discovered that there was no correlation between the Peguero-Lo Presti criterion and long-term mortality. Its sensitivity and specificity were validated by comparing it with LV mass index[10], which renders it more effective for diagnosing early ventricular remodeling. Meanwhile, it may be too sensitive for precise prediction of the occurrence of mortality that is more likely to emerge in advanced cardiac remodeling particularly among individuals with non-advanced CKD, like the present study population. The clinical significance of LVH voltage criterion in predicting mortality may need to be further evaluated in a larger, more comprehensive study.

The present study also demonstrated the association of LPFB and all-cause mortality. Even isolated LPFB is rare. Our finding was consistent with the recent report of association between isolated LPFB and long-term mortality in the study of large primary care population[32]. To the best of the authors' knowledge, no research has been done regarding to the association of fascicular block and death in CKD patients. LPFB may serve as a marker of fibrosis in the LV, which is linked to a variety of cardiac remodeling and fibrosis processes in individuals with CKD. Given the low prevalence of overall conduction disturbances observed in the present study, further research is needed to validate the findings.

The present study results emphasized the significance of baseline 12-lead ECG screening in pre-dialysis CKD patients, particularly those with cardiovascular risks. The ECG not only detected the presence of both underlying cardiomyopathy and abnormal conduction but also provided a prediction of long-term mortality. The significantly higher prevalence of ECG-indicated LVH in CKD patients may be indicative of the distinctive remodeling process in this population, which is not influenced by baseline hypertension and serves as a mortality marker in CKD.

The present study's investigation is subject to limitations. First, the limited sample size and low mortality rate may have obviated the potential association between long-term mortality and other ECG ventricular parameters. The study reported only a few cases of mortality, 13 out of 251 patients, which may restrict the generalizability of the findings, and the follow-up duration may be insufficient to notice mortality in the CKD population. An increased sample size and extended follow-up period might enhance statistical power and provide a more accurate assessment of survival outcomes. Second, the wide confidence interval of the HR for predictable abnormalities as LVH according to Cornell's criteria and LPFB, may suggest probable overfitting of the predictive factor. Third, the present study population comprised individuals with a significant risk of cardiovascular disease and renal progression, enrolled in the CORE-CKD registry, which could lead to selection bias and limit the external validity of the study's findings. Fourth, our study did not account for the progression of CKD and ECG changes during follow-up, which could impact survival outcomes. In addition, while some baseline variables were accounted for, other potential confounders such as medications, lifestyle factors, and comorbidities may not have been fully controlled in the multivariable analysis, potentially leading to biased estimates of the relationship between ECG parameters and mortality. Fifth, although ECG parameters were interpreted by two cardiologists, the potential for interobserver and intraobserver variability may still impact the consistency of the results. Nevertheless, the authors' proposed predictors were extensively used with explicitly diagnostic criterion and easily measured, thus these can be adopted for clinical application.

Conclusion

A 12-lead ECG demonstrating LVH by Cornell's voltage criteria and LPFB was associated with an increased risk of long-term all-cause mortality in pre-dialysis CKD patients with cardiovascular risks.

What is already known about this topic?

CKD patients have a higher incidence of abnormal ECG compared to the general population.

The presence of LV hypertrophy, indicated by voltage changes, can serve as a predictive factor for mortality in individuals with CKD.

What does this study add?

Presence of LV hypertrophy indicated by Cornell's criteria and left posterior fascicular block in surface ECG can predict mortality among Thai pre-dialytic CKD with cardiovascular risk.

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Authors' contributions

AP, KN performed statistical analysis, wrote the manuscript and tables. PG, PD, WW performed statistical analysis, the data analysis and data interpretation. PG, TN collected and re-checked the data prior to the analysis. KN, WW designed the cohort, conception of the data analysis, data interpretation and critically revised the manuscript. All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Conflicts of interest

All authors have no conflict of interest to declare.

References

1. Webster AC, Nagler EV, Morton RL, Masson P. Chronic kidney disease. Lancet 2017;389:1238-52.
2. Thompson S, James M, Wiebe N, Hemmelgarn B, Manns B, Klarenbach S, et al. Cause of death in patients with reduced kidney function. J Am Soc Nephrol 2015;26:2504-11.
3. Stevens PE, Ahmed SB, Carrero JJ, Foster B, Francis A, Hall RK, et al. CKD Work Group. KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int 2024;105(4S):S117-314.
4. Dobre M, Brateanu A, Rashidi A, Rahman M. Electrocardiogram abnormalities and cardiovascular mortality in elderly patients with CKD. Clin J Am Soc Nephrol 2012;7:949-56.
5. Park S, Yum Y, Cha JJ, Joo HJ, Park JH, Hong SJ, et al. Prevalence and clinical impact of electrocardiographic abnormalities in patients with chronic kidney disease. J Clin Med 2022;11:5414. doi: 10.3390/jcm11185414.
6. Braunisch MC, Gundel P, Werfel S, Mayer CC, Bauer A, Haller B, et al. Electrocardiographic parameters of left ventricular hypertrophy and prediction of mortality in hemodialysis patients. J Nephrol 2022;35:233-44.
7. Inker LA, Eneanya ND, Coresh J, Tighiouart H, Wang D, Sang Y, et al. New Creatinine- and Cystatin C-Based Equations to Estimate GFR without Race. N Engl J Med 2021;385:1737-49.
8. Casale PN, Devereux RB, Kligfield P, Eisenberg RR, Miller DH, Chaudhary BS, et al. Electrocardiographic detection of left ventricular hypertrophy: development and prospective validation of improved criteria. J Am Coll Cardiol 1985;6:572-80.
9. Sokolow M, Lyon TP. The ventricular complex in left ventricular hypertrophy as obtained by unipolar precordial and limb leads. Am Heart J 1949;37:161-86.
10. Peguero JG, Lo Presti S, Perez J, Issa O, Brenes JC, Tolentino A. Electrocardiographic criteria for the diagnosis of left ventricular hypertrophy. J Am Coll Cardiol 2017;69:1694-703.
11. Myers GB, Klein HA, Stofer BE. The electrocardiographic diagnosis of right ventricular hypertrophy. Am Heart J 1948;35:1-40.
12. Surawicz B, Childers R, Deal BJ, Gettes LS, Bailey JJ, Gorgels A, et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part III: intraventricular conduction disturbances: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society: endorsed by the International Society for Computerized Electrocardiology. Circulation 2009;119:e235-40.
13. Vink AS, Neumann B, Lieve KVV, Sinner MF, Hofman N, El Kadi S, et al. Determination and Interpretation of the QT interval. Circulation 2018;138:2345-58.
14. Bazett HC. An analysis of the time-relations of electrocardiograms. Heart 1920;7:353-70.
15. Bogossian H, Frommeyer G, Ninios I, Hasan F, Nguyen QS, Karosiene Z, et al. New formula for

evaluation of the QT interval in patients with left bundle branch block. Heart Rhythm 2014;11:2273-7.
16. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth universal definition of myocardial infarction (2018). Circulation 2018;138:e618-51.
17. Agarwal R, Light RP. Determinants and prognostic significance of electrocardiographic left ventricular hypertrophy criteria in chronic kidney disease. Clin J Am Soc Nephrol 2011;6:528-36.
18. Izumaru K, Hata J, Nakano T, Nakashima Y, Nagata M, Fukuhara M, et al. Reduced estimated GFR and cardiac remodeling: a population-based autopsy study. Am J Kidney Dis 2019;74:373-81.
19. Weber KT. Cardiac interstitium in health and disease: The fibrillar collagen network. J Am Coll Cardiol 1989;13:1637-52.
20. Kaesler N, Babler A, Floege J, Kramann R. Cardiac remodeling in chronic kidney disease. Toxins (Basel) 2020;12:161. doi: 10.3390/toxins12030161.
21. Hassan MO, Duarte R, Dix-Peek T, Vachiat A, Naidoo S, Dickens C, et al. Correlation between volume overload, chronic inflammation, and left ventricular dysfunction in chronic kidney disease patients. Clin Nephrol 2016 Suppl 1;86:131-5.
22. Briet M, Boutouyrie P, Laurent S, London GM. Arterial stiffness and pulse pressure in CKD and ESRD. Kidney Int 2012;82:388-400.
23. Law JP, Pickup L, Pavlovic D, Townend JN, Ferro CJ. Hypertension and cardiomyopathy associated with chronic kidney disease: epidemiology, pathogenesis and treatment considerations. J Hum Hypertens 2023;37:1-19.
24. London GM. Left ventricular alterations and end-stage renal disease. Nephrol Dial Transplant 2002;17 Suppl 1:29-36.
25. Miki T, Yuda S, Kouzu H, Miura T. Diabetic cardiomyopathy: pathophysiology and clinical features. Heart Fail Rev 2013;18:149-66.
26. Salman IM. Cardiovascular autonomic dysfunction in chronic kidney disease: A comprehensive review. Curr Hypertens Rep 2015;17:59. doi: 10.1007/s11906-015-0571-z.
27. Zhang H, Hu L, Wei X. Prognostic value of left ventricular hypertrophy in hypertensive patients: A meta-analysis of electrocardiographic studies. J Clin Hypertens (Greenwich) 2020;22:254-60.
28. Kim SJ, Oh HJ, Yoo DE, Shin DH, Lee MJ, Kim HR, et al. Electrocardiographic left ventricular hypertrophy and outcome in hemodialysis patients. PLoS One 2012;7:e35534.
29. Park JK, Shin JH, Kim SH, Lim YH, Kim KS, Kim SG, et al. A comparison of Cornell and Sokolow-Lyon electrocardiographic criteria for left ventricular hypertrophy in Korean patients. Korean Circ J 2012;42:606-13.
30. Xie L, Wang Z. Correlation between echocardiographic left ventricular mass index and electrocardiographic variables used in left ventricular hypertrophy criteria in Chinese hypertensive patients. Hellenic J Cardiol 2010;51:391-401.
31. Su FY, Li YH, Lin YP, Lee CJ, Wang CH, Meng FC, et al. A comparison of Cornell and Sokolow-Lyon electrocardiographic criteria for left ventricular hypertrophy in a military male population in Taiwan: the cardiorespiratory fitness and hospitalization events in armed forces study. Cardiovasc Diagn Ther 2017;7:244-51.
32. Nyholm BC, Ghouse J, Lee CJ, Rasmussen PV, Pietersen A, Hansen SM, et al. Fascicular heart blocks and risk of adverse cardiovascular outcomes: Results from a large primary care population. Heart Rhythm 2022;19:252-9.