ORIGINAL ARTICLE

Relationship of Electrocardiographic Left Ventricular Hypertrophy to the Presence of Diastolic Dysfunction

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Background: Left ventricular (LV) diastolic dysfunction (DD) is a known predictor of poor cardiovascular outcomes. Although ECG LV hypertrophy (LVH) is strongly associated with LV systolic dysfunction and heart failure, the relation of LV DD to ECG LVH is unclear.

Methods: ECG LVH by Cornell product (CP) criteria was examined in a cohort of 185 patients who underwent both cardiac computed tomographic angiography and transthoracic echocardiography with complete evaluation of diastolic function. The presence of DD was determined via evaluation of mitral inflow velocities, tissue Doppler imaging, deceleration time, isovolumic relaxation time, pulmonary venous systolic: diastolic ratio, and left atrial enlargement.

Results: Among the 185 patients (56% female, mean age 54.6 ± 15.6), 105 (57%) had DD. In univariate logistic regression analysis, patients in the upper quartile of CP (≥1595 mm·ms) had a >5-fold greater odds of DD (odds ratio [OR] 5.1, 95% confidence interval [CI] 2.2–11.7, $P < 0.001$). In alternative analyses treating CP as a continuous variable, each 1 SD increase in CP (664 mm·ms) was associated with an OR of 1.9 for DD (95% CI 1.3–2.7, $P < 0.001$). In multivariate logistic regression analyses adjusting for univariate predictors of DD, the highest quartile of CP remained associated with a 5.9-fold increased odds of DD (95% CI 2.3–15.4, $P = 0.001$), and each 1 SD of CP with a 1.7-fold increased odds of DD (95% CI 1.2–2.5, $P = 0.005$).

Conclusions: CP LVH is a strong predictor of DD, even after adjustment for other potential risk factors and ECG variables.

Ann Noninvasive Electrocardiol 2014;19(6):552–560

electrocardiography; hypertrophy; diastolic dysfunction; heart failure

The presence of abnormal left ventricular (LV) diastolic filling as evaluated by echocardiography is an established independent predictor of cardiovascular morbidity and mortality.[1,2] Nearly half of all patients with congestive heart failure (CHF) have impaired ventricular relaxation with a preserved ejection fraction, and diastolic dysfunction (DD) is prevalent in the community. However, many patients with DD are asymptomatic before the development of clinical symptoms of heart failure,[3] making accurate and cost-effective means of detection a priority.[4] Pharmacologic interventions and lifestyle modifications are critical, as worsening of diastolic function in patients with either normal or impaired diastolic function at baseline has been shown to be an independent predictor of mortality.[5]

Left ventricular hypertrophy (LVH), as measured by indexed LV mass on echocardiography, is associated with impaired diastolic function,[6]

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Disclosures: Dr. Krepp, none. Dr. Lin, none. Dr. Min has research grants from GE Healthcare, Merck, Guerbet, and Philips Medical, serves on the advisory boards for Abbott Vascular, Astra Zeneca, GE Healthcare, and Arineta and has ownership interest in MDDX, TC3, and AutoPlaq. Dr. Devereux serves on advisory boards for Merck, Novartis, Sanofi-Aventis, GE Healthcare, and Edwards Lifesciences. Dr. Okin serves as a consultant to and has research grants from Novartis and serves on a medical advisory board for GE Medical Systems.

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DOI:10.1111/anec.12166

especially in patients with hypertension and concentric hypertrophy.[7] The principle mechanisms via which LVH adversely affects diastolic function are thought to be abnormalities in LV active relaxation and passive stiffness.[8] Long-term follow-up from Framingham shows that patients diagnosed with LVH by either echocardiogram or electrocardiogram (ECG) are at a substantially higher risk of cardiovascular events.[9,10] Although limited data suggest a relationship of QT interval prolongation to DD,[11] to date, the relation between standard 12-lead ECG criteria for LVH and impaired diastolic function has not been assessed. Therefore, this study was undertaken to evaluate the performance of commonly utilized ECG criteria for LVH for detection of echocardiographic DD.

METHODS

Study Population

One hundred eighty-five patients were selected from a database of 444 patients who underwent both cardiac computed tomographic angiography (CCTA) and transthoracic echocardiography (TTE) because all had undergone complete evaluation of diastolic function. Subjects were excluded from enrollment at the time of TTE if they met any of the following criteria: LV ejection fraction <45%, significant valvular disease, hypertrophic cardiomyopathy, pericardial constriction, congenital heart disease, primary pulmonary hypertension, pulmonary embolism, and atrial or ventricular arrhythmias. Two hundred sixteen patients were identified who underwent ECG within 1 year of TTE at New York Presbyterian Hospital-Weill Cornell Medical Center from 2005 to 2010. Patients were further excluded because of the presence of a left bundle branch block (n = 6), right bundle branch block (n = 14), ventricular paced rhythm (n = 6), or atrial arrhythmia (n = 3). After initial analysis, subjects with restrictive DD (n = 2) were also excluded due to a low prevalence in the study population. Patients provided their medical history and cardiovascular risk factors via questionnaire, and referring diagnoses for TTE were also collected.

Echocardiography

All subjects underwent complete M-mode imaging, two-dimensional and color Doppler echocardiography, tissue Doppler imaging of the septal and lateral mitral annulus, pulse wave Doppler assessment of mitral inflow, and continuous-wave Doppler evaluation of tricuspid flow.[12] Studies were interpreted by echocardiographers blinded to ECG data. Abnormalities in LV diastolic function were assessed using the following: the ratio of mitral early (E) and late (A) velocities, septal tissue Doppler early (E′) velocity, along with abnormalities in deceleration time, isovolumic relaxation time, pulmonary venous S:D ratio, and left atrial size according to standard guidelines.[12–14] Using standardized principles, each subject's diastolic function was graded as normal (Stage I), abnormal relaxation (Stage II), pseudonormal (Stage III), and restrictive (Stage IV).[12–14] In addition, an estimate of LV diastolic pressure (LVEDP) was calculated using the following formula: LVEDP = 4 + E/E′.[12,15] LV mass was calculated using an autopsy-validated formula[16] and indexed to body surface area.

Cardiac Computed Tomographic Angiography

Coronary artery disease (CAD) was evaluated by CCTA by scoring the maximal per-patient and per-segment intraluminal stenosis over the 18-segment Society of Cardiovascular Computed Tomography model (0 = none, 1 = 1–49%, 2 = 50–69%, and 3 = 70–100%). Coronary plaque was classified as calcified, noncalcified, or mixed (30–70% admixture of both calcified and noncalcified components). A stenosis-weighted sum of affected segments was calculated to obtain a segment stenosis score (SSS) as a semiquantitative measure of plaque burden (maximum = 54) and plaque composition scores by adding the number of segments exhibiting each plaque composition (maximum = 18).

Electrocardiography

Standard 12-lead ECGs were recorded by skilled ECG technicians at 25 mm/s and 1 mV/cm according to standard American Heart Association recommendations[17] and their results were interpreted by one of two physicians who were blinded to TTE results. Digital ECGs performed within 1 year of TTE were identified via chart review. All subjects whose ECG demonstrated sinus rhythm and did not meet any of the

ECG or TTE exclusion criteria were included for analysis. If more than one ECG was available, the ECG closest in time to TTE was selected for analysis. ECG measurements performed using MUSE software 005C (GE Healthcare, Milwaukee, WI, USA) included QRS duration and axis, and the PR, QT, and QTc intervals. LVH was calculated using sex-specific Cornell product (CP) criteria: [sum of the R wave in aVL plus the S wave in V_3, plus 6 mm in women] × QRS duration; as well as Cornell Voltage (CV) criteria: sum of the R wave in aVL plus the S wave in V_3.[18,19] Sokolow-Lyon voltage (SLV) (sum of the amplitude of the S wave in V_1 and the greatest R wave in either V_5 or V_6) was also calculated.[20] ST depression was measured in leads V_5 and V_6 at the midpoint between the J-point and the end of the ST segment, with the maximum value used for analysis. Left and right bundle branch blocks were identified using Minnesota Coda criteria.[21] A composite marker of conduction, termed incomplete block, was diagnosed in the presence of left anterior or posterior fascicular block or incomplete right or left bundle branch block. All ECG variables were recorded by a physician independent of ECG or TTE interpretation.

Statistical Analyses

All statistical analyses were performed using SPSS, version 19.0 (SPSS Inc., Chicago, IL, USA) with a 2-tailed $P < 0.05$ considered statistically significant. Data are presented as mean ± SD for continuous variables and as percentages for categorical variables. Chi-square tests and independent *t*-tests were used for comparison of categorical and continuous variables, respectively. Univariate logistic analyses were used to establish the relationship between DD and individual independent variables. Multivariate logistic regression models using a forward stepwise approach were constructed using significant correlates of impaired diastolic function in univariate analyses.

ECG LVH by CP criteria was evaluated as a categorical variable by dividing subjects into the highest quartile (≥1595 mm·ms) versus the lower three quartiles or evaluated as a continuous variable. Odds ratios (ORs) for the likelihood of having DD for CP as a continuous variable were calculated per 1 SD higher CP as the antilog of the estimated coefficient times 664. Similar computations were performed for incremental increases in other ECG variables, CV, SLV, indexed LV mass, and age. The 95% confidence interval (CI) of each OR was calculated from the estimated coefficients and standard errors.

RESULTS

Study Group

One hundred eighty-five patients met the study's selection criteria, of which 105 (57%) had DD diagnosed by TTE. The mean time between ECG and TTE was 105 ± 110 days. Characteristics of all subjects and the comparison between those with and without DD are listed in Table 1. Of the 185 patients, 104 (56%) were women and the mean age was 54.6 ± 15.6 years. Compared with subjects without DD, those with DD were on average older and had higher prevalence of hypertension and hypercholesterolemia. Patients did not differ with respect to gender, body mass index (BMI), smoking status, diabetes, or family history of CAD. Subjects with DD had higher prevalence of dyspnea and a murmur on clinical exam as primary indications for TTE while those without DD had a higher prevalence of chest pain.

ECG and echocardiographic data in relation to presence or absence of DD are presented in Table 2. In the overall population, mean CP was 1240 ± 664 mm·ms and mean SLV was 19.8 ± 8.4 mm. Compared with patients without DD, those with DD had a more leftward QRS axis, longer PR interval, higher prevalence of incomplete block, higher mean CP and CV as well as a higher prevalence of both CP-LVH and CV-LVH, but there was no difference in the two groups with respect to SLV-LVH. As expected from criteria for group assignment, subjects with DD had more abnormal E/A ratio, deceleration time, septal E′, E/E′, and higher mean estimated LVEDP; they also had slightly higher indexed LV mass. There was no difference in LV ejection fraction or LV internal diastolic dimension between groups. CCTA data in relation to presence or absence of DD are presented in Table 3. Compared with subjects without DD, those with DD had greater coronary calcium scores, more significant CAD burden, and greater SSS. Of note, patients with stages II and III DD did not differ significantly with respect to any of the clinical, demographic, or ECG variables shown in Tables 1 and 2.

Table 1. Characteristics of Patients Stratified by Presence of Diastolic Dysfunction

	No Diastolic Dysfunction (N = 80)	Diastolic Dysfunction (N = 105)	P-Value
Age (years)	46.3 ± 14.4	61.0 ± 13.4	<0.001
Gender (% male)	43.8%	43.8%	1.000
BMI in kg/m^2 (SD)	27.8 ± 6.3	28.6 ± 6.4	0.367
Hypertension (%)[a]	51.2%	68.6%	0.022
Hypercholesterolemia (%)[b]	37.5%	61.0%	0.002
Diabetes (%)[b]	10.0%	16.2%	0.280
Smoking			
Current (%)	20.0%	17.1%	0.703
Former (%)	18.8%	17.1%	0.847
Coronary artery disease (%)[c]	25.0%	33.0%	0.257
Family history CAD (%)	15.0%	20.0%	0.441
Indication for echocardiogram			
Dyspnea (%)[d]	12.5%	24.8%	0.041
Chest pain (%)	41.3%	23.8%	0.016
Murmur on clinical exam (%)	3.8%	13.3%	0.038
Other (%)[e]	42.5%	38.1%	0.549

[a]Hypertension defined as systolic blood pressure greater than 140 mmHg or diastolic blood pressure greater than 90 mmHg or treatment with antihypertensive medications;
[b]Hypercholesterolemia defined as patient reported history of hypercholesterolemia or diagnosis in the medical record; diabetes defined as patient reported history of diabetes or diagnosis in the medical record;
[c]Coronary artery disease defined as history of greater than 50% coronary artery stenosis through invasive or noninvasive imaging, history of percutaneous coronary intervention, coronary artery bypass grafting, myocardial infarction, or history of abnormal stress consistent with ischemia;
[d]Subjects referred for congestive heart failure were included with Dyspnea;
[e]Other indications included syncope, pericarditis, hypertension, palpitations, and coronary artery disease.

Prediction of DD

Univariate logistic regression analyses were performed for all potential clinical and ECG predictors of DD (Table 4). Statistically significant clinical predictors of DD included age, hypertension, and hypercholesterolemia while significant ECG predictors included longer PR interval, leftward QRS axis, incomplete block, maximal ST-depression in leads V_5 or V_6, CV-LVH, and CP LVH. In treating CP as a continuous variable, each 1 SD increase was associated with an OR of 1.9 for DD (95% CI 1.3–2.7, $P < 0.001$). Being in the upper quartile of calculated CP (≥1595 mm·ms) was associated with a significantly higher prevalence of DD (82.6% vs. 48.2%, $P < 0.001$) and with more than fivefold increased odds of having DD (OR 5.1, 95% CI 2.2–11.7, $P < 0.001$). In parallel analyses, each 1 SD increase of CV was associated with an OR of 2.0 for DD (95% CI 1.4–2.8, $P < 0.001$) and being in the upper quartile of calculated CV (≥17.5 mm) was associated with an OR of 4.3 for DD (95% CI 1.9–9.6, $P < 0.001$). Being in the upper quartile of calculated CP (a calculated CP >1595 mm·ms) had a sensitivity of 36.0%, specificity of 90.0%, positive predictive value of 82.6%, and a negative predictive value of 51.8% for the detection of DD.

SLV, gender, BMI, heart rate, corrected QT interval, and QRS duration were not significantly associated with DD, although QRS duration trended toward significance. Although indexed LV mass was associated with an increased odds of DD when treated as a continuous variable, being in the upper quartile was not associated with an increased odds of having DD. CAD burden, represented by SSS had a significant association with DD. Being in the upper quartile of SSS (≥11 points) was associated with an OR of 8.2 for DD (95% CI 3.3–20.6, $P < 0.001$) and when evaluated as a continuous variable, each 1 SD increase in SSS was associated with an OR of 3.1 (95% CI 1.9–4.9, $P < 0.001$).

Since subjects with and without DD differed with respect to several independent variables, the relationship of CP LVH to DD was evaluated by adjusting for these variables using a forward, stepwise multivariate logistic regression analysis (Table 5). The relationship of DD to CP LVH was evaluated in separate models treating CP LVH as either a continuous or categorical variable. After adjustment for statistically significant univariate predictors of DD including age, history of hypertension, hypercholesterolemia, indexed LV mass, SSS, R-wave axis, PR interval, and ST-segment

Table 2. Electrocardiographic and Echocardiographic Results in Relation to Presence of Diastolic Dysfunction

	No Diastolic Dysfunction (N = 80)	Diastolic Dysfunction (N = 105)	P-Value
Electrocardiographic data			
Heart rate (beats/min)	71.1 ± 14.1	68.7 ± 13.0	0.234
QRS axis (deg)	34.4 ± 29.3	16.7 ± 33.5	<0.001
QRS duration (ms)	86.6 ± 8.4	89.3 ± 10.4	0.060
PR interval (ms)	155.0 ± 22.7	164.9 ± 33.0	0.021
QT interval (ms)	397.7 ± 33.4	407.7 ± 39.0	0.068
QTc interval (ms)	426.4 ± 25.7	421.8 ± 57.9	0.515
Cornell product LVH (%)	1.3%	7.6%	0.080
Cornell product (mm·ms)	1030 ± 539	1400 ± 707	<0.001
Cornell voltage LVH (%)	1.3%	12.4%	0.004
Cornell voltage (mm)	11.5 ± 5.0	15.3 ± 7.0	<0.001
Sokolow-Lyon voltage LVH (%)	3.8%	1.9%	0.654
Sokolow-Lyon voltage (mm)	20.2 ± 8.6	19.4 ± 8.3	0.500
Incomplete block (%)*	1.3	10.5	0.026
Echocardiogram data			
Ejection fraction	64.3 ± 7.1	63.4 ± 7.0	0.427
E/A ratio (N = 171)	1.4 ± 0.4	1.0 ± 0.3	<0.001
Septal E′ (cm/s)	10.2 ± 2.2	6.3 ± 2.3	<0.001
Septal E/E′ ratio (N = 176)	8.5 ± 2.5	13.9 ± 6.4	<0.001
Estimated LVEDP (N = 176)	12.5 ± 2.5	17.9 ± 6.4	<0.001
Deceleration time (ms) (N = 157)	181.5 ± 33.6	229.2 ± 64.0	<0.001
Left atrial volume index (mL/m^2) (N = 88)	29.6 ± 11.2	31.3 ± 7.3	0.401
Left ventricular mass index (g/m^2)	82.4 ± 17.6	89.1 ± 16.6	0.008
Left ventricular internal diastolic dimension (mm)	50.4 ± 0.5	50.8 ± 0.5	0.570
Relative wall thickness	0.33 ± 0.05	0.35 ± 0.05	0.012
Left ventricular hypertrophy (%)	2.5%	5.7%	0.470
Stage of diastolic function			
I (normal)	100%	-	
II (impaired relaxation)	-	44.8%	
III (pseudonormal)	-	55.2%	

*Incomplete block defined as presence of either left anterior or posterior fascicular block, left or right incomplete bundle branch block.

deviation as covariates, the highest quartile of CP showed a robust and statistically significant increased odds of having DD (OR 5.9, 95% CI 2.3–15.4, $P < 0.001$). In parallel analyses treating CP as a continuous variable and adjustment for covariates each 1 SD increase of CP was associated with a 1.7-fold increased odds of DD (95% CI 1.2–2.5, $P = 0.005$). In both models, age, SSS, and hypercholesterolemia were the only other variables that remained independently associated with DD. Of note, CP LVH had similar predictive value for prediction of stage II or stage III DD in separate multivariate logistic models (data not shown).

DISCUSSION

This study demonstrates that increased ECG LVH by CP is strongly associated with the presence of echocardiographic DD in patients with a preserved ejection fraction. The highest quartile of CP ECG LVH, compared to the lower three quartiles, was associated with a nearly sixfold higher odds of DD and this relationship persisted after adjustment for clinical and ECG covariates. Both univariate and multivariate analyses demonstrated a stronger association of DD with CP LVH than with SL LVH or other potential ECG markers of DD including heart rate, QRS duration, corrected QT interval, PR interval, ST deviation, and QRS axis. These findings suggest that increased CP LVH can identify patients in need of further cardiovascular evaluation of possible underlying DD.

CP LVH and DD

Limited data exist concerning electrocardiographic markers of impaired diastolic function; whereas in the case of LV systolic dysfunction, ECG variables play critical roles in diagnosis and

Table 3. Coronary Cardiac CT Angiogram Results in Relation to Presence of Diastolic Dysfunction

	No Diastolic Dysfunction (N = 80)	Diastolic Dysfunction (N = 105)	P-Value
Maximum vessel stenosis			
No plaque (%)	56.3%	20.0%	<0.001
1–49% (%)	25.0%	27.6%	0.739
50–69% (%)	11.3%	9.5%	0.808
70–100% (%)	7.5%	42.9%	<0.001
Number of obstructive vessels			
None	81.3%	47.6%	<0.001
1-vessel disease	7.5%	12.4%	0.334
2-vessel disease	7.5%	25.7%	0.002
3-vessel disease or left main disease	3.8%	14.3%	0.022
Segment stenosis score	2.7 ± 5.1	8.8 ± 8.7	<0.001
Coronary calcium score (N = 114)			
0, N (%)	31 (63.3%)	18 (27.7%)	<0.001
1–100, N (%)	12 (24.5%)	23 (35.4%)	0.227
>100, N (%)	6 (12.2%)	24 (36.9%)	0.005

Table 4. Univariate Predictors of Diastolic Dysfunction

Variable	OR	95% CI	P-Value
Age, per 10 year	2.05	1.61–2.62	<0.001
Male sex	1.00	0.56–1.79	0.994
Body mass index, per kg/m^2	1.02	0.98–1.07	0.366
Hypertension	2.08	1.14–3.79	0.017
Hypercholesterolemia	2.60	1.43–4.74	0.002
Heart rate, per 10 bpm	0.88	0.71–1.09	0.233
QRS duration, per 10 ms	1.33	0.98–1.82	0.068
QTc interval, per 10 ms	0.98	0.91–1.05	0.519
PR interval, per 10 ms	1.15	1.02–1.29	0.024
R-wave axis, per 10° leftward	1.19	1.08–1.32	<0.001
Maximum ST depression, per 10 μV	1.11	1.01–1.22	0.026
Cornell product, per SD (664 mm·ms) increase	1.91	1.34–2.70	<0.001
Cornell product 75th percentile (≥1595 mm·ms)	5.10	2.22–11.73	<0.001
Cornell voltage, per SD (6.5 mm) increase	1.96	1.39–2.77	<0.001
Cornell voltage 75th percentile (≥17.5 mm)	4.29	1.93–9.56	<0.001
Sokolow-Lyon voltage, per 5 mm	0.94	0.79–1.12	0.497
Incomplete block	9.25	1.17–73.10	0.035
Left ventricular mass index, per 5 g/m^2	1.13	1.03–1.23	0.010
Segment stenosis score, per SD (8.0 point) increase	3.06	1.85–4.91	<0.001
Segment stenosis score 75th percentile (≥11)	8.22	3.28–20.61	<0.001

management.[22–24] A recent study of consecutive patients referred for a clinical suspicion of heart failure demonstrated that QT interval lengthening was associated with worsening diastolic function as defined by E′ velocity but found no significant relationship between reduced E′ velocity and LVH on the ECG.[11] However, this study did not define the ECG LVH criterion used in the analysis, and differences in the study populations such as including only patients with suspected heart failure as well as those with left or right bundle branch blocks are possible explanations for the differing results between the current and previous study. Previous data from the Losartan for Intervention for Endpoint Reduction in Hypertension (LIFE) Study investigators have demonstrated that regression of CP LVH is associated with decreased hospitalizations secondary to heart failure among hypertensive patients,[25] suggesting a possible relationship of changing levels of CP LVH to changing diastolic function. However, the small number of patients with new heart

Table 5. Multivariate Model for Prediction of Diastolic Dysfunction

Variable	OR	95% CI	P-Value
Model with Cornell product 75th percentile*			
Age, per 10 year increase	1.71	1.31–2.24	<0.001
Cornell Product 75th percentile (≥1595 mm·ms)	5.91	2.27–15.42	<0.001
Segment stenosis score 75th percentile (≥11 points)	4.11	1.44–11.74	<0.001
Hypercholesterolemia	2.66	1.28–5.52	0.009
Model with Cornell product as continuous variable*			
Age, per 10 year increase	1.69	1.28–2.24	<0.001
Cornell product, per SD (664 mm·ms) increase	1.71	1.18–2.48	0.005
Segment stenosis score, per SD (8.0 point) increase	1.73	1.07–2.78	0.024
Hypercholesterolemia	2.46	1.21–4.99	0.013

*Adjusted for statistically significant univariate predictors of diastolic dysfunction including age, history of hypertension, hypercholesterolemia, indexed LV mass, R-wave axis, PR interval, and ST-segment deviation as covariates.

failure who had echocardiographic assessment of systolic and diastolic function as part of the LIFE echocardiographic substudy (about 11% of the study population) did not allow for meaningful assessment of the possible contribution of DD to this relationship.

Electrocardiographic criteria for LVH are well-established predictors of cardiovascular morbidity and mortality.[10,26–29] Prognostic implications of ECG LVH were established in early analyses in the Framingham Heart Study cohort, in which subjects with ECG LVH had a significantly increased risk of developing coronary heart disease.[26,29] The LIFE Study demonstrated that changing levels of CP LVH during antihypertensive treatment predict cardiovascular mortality, stroke, myocardial infarction, new onset atrial fibrillation, and the risk of developing new diabetes.[30–32] In addition, a recent study from Japan found that stroke risk was increased in patients with ECG CP LVH.[33] The strong association of CP LVH with DD in the current study raises the intriguing possibility that some of the prognostic value of CP LVH may be mediated via this association. Further study of the relative prognostic value of DD and CP LVH in populations undergoing both electrocardiography and echocardiography will be required to more fully evaluate this possibility.

In addition to prior studies that demonstrated the predictive implications of ECG CP LVH exceeding the diagnostic threshold value of 2440 mm·ms, the present study demonstrates that solely having a calculated ECG CP ≥1595 mm·ms (defining the upper quartile of values in the current population) had over a fivefold increased odds of having DD compared with a lower CP. In addition, the strong association of increased CP with DD was not dependent on use of the 75th percentile threshold partition, as CP examined as a continuous variable was a highly significant predictor of DD. Importantly, the strong predictive power of ECG CP remained in both univariate and multivariate analysis, further demonstrating the utility of using ECG CP as a predictor of impaired diastolic function.

The association of ECG CP and DD cannot be fully explained by increased LV mass, as indexed LV mass showed a weak correlation with DD as a continuous variable and was not a predictor of DD in the multivariate analyses. It can be hypothesized that the link between CP and DD is closely related to the presence of myocardial fibrosis with resultant impaired ventricular conduction. Through the use of cardiovascular magnetic resonance, myocardial fibrosis has been demonstrated to be closely associated with the presence of LVH.[34] In addition, it has been established that a pattern of diffuse myocardial fibrosis in patients with hypertrophic cardiomyopathy is predictive of the presence of DD.[35] Further studies utilizing cardiovascular magnetic resonance would be necessary to establish a relationship between CP LVH, myocardial fibrosis, and DD.

With rising healthcare costs and Medicare expenditure, appropriate test utilization has gained significant attention in recent years. While rising costs are multifactorial, the use of cardiovascular imaging modalities, particularly echocardiography, has increased at a rate consistent with that of national healthcare costs, and with an aging population these expenses will continue to rise.[36] Identification of patients who warrant cardiovascular imaging based upon clinical and evidence-based criteria is both a clinical and economic necessity.[37]

Risk factors for DD, including increasing age and hypertension, will only increase in prevalence in our population making it challenging to identify those patients who warrant further imaging. The data in the present study demonstrate that the widely accessible and inexpensive ECG is a diagnostic tool that can identify patients with increased odds of having DD, and those patients who should appropriately undergo echocardiographic evaluation of their diastolic function. The predictive power of CP LVH for the detection of DD (positive predictive value 83%, specificity 90%) can be further strengthened by applying these criteria in patients at increased risk of DD based on increasing age and hypertension. Patients who present with symptoms consistent with heart failure and have a calculated CP $\geq$1595 mm·ms would benefit from further assessment of their diastolic function as a diagnosis of DD should be considered.

The information presented in the current study should not replace the use of diagnostic echocardiography in the evaluation of patients' diastolic function, but rather be used to identify those patients with increased likelihood of having impaired diastolic function. Investigators have previously evaluated alternative means of detection of DD by relating subjects' brain natriuretic peptide (BNP) levels to their degree of DD.[38–41] BNP levels were highly correlated with DD in patients in clinical settings as well as those with clinically evident heart failure and a restrictive pattern on echocardiogram;[39,40] however, BNP was a poor diagnostic tool in an asymptomatic general population.[41] The wide use of the standard 12-lead ECG provides clinicians with a novel avenue to identify patients who would benefit from more aggressive treatment and risk reduction if echocardiography identified diastolic function.

Study Limitations

The relationship between increased calculated CP LVH and presence of DD in the current study relates to impaired relaxation and pseudonormal LV filling, and may not be applicable to patients with restrictive diastolic physiology. The current study is retrospective in nature, and selection and referral bias may be present in a population of patients who underwent both CCTA and echocardiographic analysis of DD for clinical indications. The nonsimultaneous performance of ECGs and TTEs may introduce noise into the relationship between variables. Finally, blood pressure measurements, serum creatinine, and current medications were not available and could not be included as covariates for analyses.

CONCLUSIONS

This study is the first of which we are aware to demonstrate that ECG LVH, as defined by CP, is an independent correlate of DD. These findings suggest that higher levels of CP LVH are associated with the development of DD. Further follow-up studies are needed to assess the predictive value of CP LVH for DD in larger and more heterogeneous populations at risk of having DD.

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