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Association of vitamin D deficiency with electrocardiographic markers of left atrial abnormalities

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Abstract

Objective: Electrocardiographic markers of left atrial (LA) abnormalities are linked to increased risk of cardiovascular disease (CVD). We examined the relationship of vitamin D deficiency with prolonged P wave duration and PR interval as markers of LA abnormalities.

Methods: This analysis included 5,894 participants (58.12 ± 12.9 years; 54.7% women; 49.8% non-Hispanic Whites) without clinical CVD from NHANES III. A multivariable logistic regression model was used to examine the association of vitamin D categories (<20 ng/ml, 20–29 ng/ml and >30 ng/ml (reference) with prolonged P wave duration (≥120 ms) and PR interval (≥200 ms).

Results: There was an incremental increase in the prevalence of prolonged P wave duration and PR interval across vitamin D categories with the highest prevalence in study participants with vitamin D levels <20 ng/ml, followed by 20–29 ng/ml and then >30 ng/ml (trend p-value < 0.0001). Vitamin D deficiency (<20 ng/ml) was associated with prolonged P wave duration (OR [95% CI]: 1.22 [1.03–1.45], $p = 0.02$) and prolonged PR interval (OR [95% CI]: 1.48 [1.12–1.97], $p = 0.006$) in multivariable logistic regression models adjusted for demographics, CVD risk factors, and other potential confounders. These associations were consistent across subgroups stratified by age, sex, and race.

Conclusions: Vitamin D deficiency is associated with an increased risk of LA abnormalities. This association elucidates an alternate pathway through which vitamin D deficiency may increase CVD risk. Whether vitamin D supplementation would improve LA abnormalities requires further investigation.

KEYWORDS
NHANES III, P wave duration, PR interval, vitamin D

1 | INTRODUCTION

Association of vitamin D deficiency with cardiovascular disease (CVD) has been established (Theodoratou, Tzoulaki, Zgaga, & Ioannidis, 2014). Low levels of serum 25(OH)D are associated with prevalent coronary heart disease (Kendrick, Targher, Smits, & Chonchol, 2009) as well as incident CVD (Wang et al., 2008). On the other hand, the association between vitamin D deficiency and atrial fibrillation (AF) is not as established; some studies reported an increased risk of AF with 25(OH)D deficiency (Chen et al., 2014; Ozcan, Gurlek, Gursoy, Gerede, & Erol, 2015) while others reported no association (Alonso et al., 2016; Vitezova et al., 2015).

Prolonged P wave duration and PR interval are established markers of abnormal atrial conduction, reflecting impaired inter-atrial conduction secondary to chamber enlargement and fibrotic remodeling of atrium (Ariyarajah, Mercado, Apiyasawat, Puri, & Spodick, 2005; Cheng et al., 2009), and both have been independently associated with incidence and recurrence of AF, all-cause, and CVD mortality (Cheng et al., 2009; Magnani, Gorodeski et al., 2011; Magnani, Johnson et al., 2011). Therefore, prolonged P wave and PR interval serve as markers of poor outcomes, and examining associations of these electrocardiographic (ECG) intervals with risk factors provide insight into increased risk associated with these risk factors.

To our knowledge, there have been no population-based studies evaluating the association of vitamin D deficiency with left atrial abnormalities. Therefore, we sought to examine cross-sectional association of levels of serum 25(OH)D with P wave and PR interval in a sample from the third National Health and Nutrition Examination Survey (NHANES III) free of CVD. We hypothesized that low 25(OH)D levels (<20 ng/ml) would be associated with prevalent prolonged P wave duration and PR interval independent of lifestyle and CVD risk factors.

2 | METHODS

2.1 | Study participants

We analyzed data from the Third National Health and Nutrition Examination Survey (NHANES III), a cross-sectional study conducted between 1988 and 1994 that used a multistage stratified clustered probability design to select a representative sample of the civilian noninstitutionalized US population ("Plan and operation of the Third National Health and Nutrition Examination Survey, 1988-94. Series 1: programs and collection procedures", 1994). The NHANES III study was approved by the National Center for Health Statistics (NCHS) Research Ethics Review Board, and documented consent was obtained from participants. Between 1988 and 1994, initial home interviews were conducted to collect baseline information, including demographics (age, sex, race), medication data (e.g., use of antihypertensive), past medical history (e.g., history of CVD), and behavioral data (e.g., smoking). Subsequently, participants visited mobile examination centers and gave blood samples to record basic laboratory values for each participant (e.g., total cholesterol [TC], plasma glucose).

2.2 | Measurement of vitamin D

In the NHANES III, serum 25-OH vitamin D was measured by a radioimmunoassay (RIA) kit after extraction with acetonitrile (DiaSorin, Stillwater, MN) by the National Center for Environmental Health, Centers for Disease Control and Prevention (Atlanta, GA). The kit manufacturer reformulated the kit in the late 1990s by introducing an antibody that improved binding. To assess the magnitude of change of the reformulated assay on the originally measured 25-OH vitamin D in NHANES III, the CDC laboratory reanalyzed a subset of 150 samples representative of the entire NHANES III population using the reformulated assay, and the results were regressed using the following equation: 25-OH vitamin D (corrected 2004 RIA) = 0.8429 × 25-OH vitamin D (1988–1994 RIA) + 2.5762 (nmol/L) (Yetley et al., 2010). We categorized vitamin D levels as (a) <20 ng/ml, (b) 20–29 ng/ml, and (c) ≥30 ng/ml (reference) (Holick et al., 2011; Hossein-nezhad & Holick, 2013).

2.3 | Electrocardiogram

Resting 12-lead ECG were obtained with a Marquette MAC 12 system (Marquette Medical Systems, Milwaukee, WI) during the mobile examination visits by trained technicians. Analysis of ECG was achieved through a computerized automated process and visual inspection by a trained technician located in a centralized core laboratory. PR interval and P duration in lead II were automatically measured among other ECG measurements. P wave duration was measured from the onset of the P wave to the end of the P wave. PR interval was measured from the beginning of the P wave to the beginning of the QRS. Given dependence of PR interval on heart rate (HR), PR interval was adjusted using the formula: PRa = PR + 0.26 (HR − 70) for age group younger than 60 years and PRa = PR + 0.42 (HR − 70) for age group 60 years or older (Soliman & Rautaharju, 2012). Heart rate-adjusted prolonged PR was defined as PR interval ≥200 ms. Prolonged P wave duration was defined as P wave ≥120 ms.

2.4 | Measurement of other variables

In the home interview, demographic information regarding age, sex, race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American, and other), income (<$20,000/year and >$20,000/year), smoking status (never, current, and former), alcohol intake (<12 drinks in the lifetime or lifetime abstainers and ≥12 drinks over the lifetime including both current and former drinkers), and leisure time physical activity (number of times engaged in physical activity in past month) was collected. Height was measured using a wall-mounted stadiometer, and weight was measured using a Toledo digital scale in minimal clothing. BMI was calculated from height and weight measurements. Blood pressure (mmHg) was measured three times during the in-home interview and three additional times during the participant's visit to the mobile examination center. Blood samples were collected via venipuncture by a phlebotomist. Samples were analyzed for TC, serum creatinine, c-reactive protein (CRP), and glucose, using laboratory procedures as reported by NCHS.

For this study, we only considered NHANES III participants who underwent an ECG recording (n = 8,561). We excluded participants with a history of CVD (myocardial infarction, heart failure, or stroke), without sinus rhythm, any major abnormalities on their electrocardiograms according to the Minnesota Code classification (Prineas, Crow, & Zhang, 2010), and missing key covariates. After all

exclusions (n = 2,667), 5,894 participants were included in the final analysis.

2.5 | Statistical analysis

Baseline characteristics were compared across three vitamin D categories (≥30 ng/ml, 20–29 ng/ml, and <20 ng/ml). Continuous variables were reported as mean ± standard deviation (*SD*) while categorical variables were reported as frequency and percentage. Analysis of variance (ANOVA) was used to compare the continuous variables while chi-square was used to compare the categorical variables. Multivariable logistic regression analysis was used to compute odds ratios and 95% confidence interval (CI) for the cross-sectional association of each vitamin D category (≥30 [reference], 20–29, and <20) with prolonged P wave duration and prolonged PR interval separately. We also performed multivariable linear regression analysis with vitamin D categories (≥30 [reference], 20–29, and <20) as the independent variable while P wave duration and PR interval as the outcome variable to compute beta-coefficient and 95% confidence interval separately. In both approaches, Model 1 was adjusted for age, sex, race, and socioeconomic status, model 2 adjusted for model 1 plus smoking and physical activity, BMI, and alcohol intake, and model 3 adjusted for model 2 plus systolic blood pressure, diastolic blood pressure, antihypertensive medications, insulin resistance, TC, C-reactive protein, serum phosphorus, estimated glomerular filtration rate, and urine albumin/creatinine ratio.

As an additional analysis, we conducted subgroup analysis stratified by age (using 65 years as a cut point), sex, and race (whites vs. nonwhites). The models were adjusted in a similar fashion to model 3 as mentioned above.

All statistical analyses were performed using with SAS version 9.4 (SAS Institute Inc, Cary, NC), and p-values were considered significant if <0.05.

3 | RESULTS

This analysis included 5,894 participants (58.12 ± 12.9 years; 54.7% women; 49.8% non-Hispanic Whites). Table 1 shows baseline characteristics of participants by vitamin D categories. Vitamin D deficient was more likely to be young, woman, nonwhite, current smoker, belonged to low income level and to have more CVD risk factors like high systolic blood pressure, higher body mass index, lower physical activity levels, higher C-reactive protein levels, and higher prevalence of insulin resistance. Prolonged P wave duration and PR interval were present in 23.7% and 6.9% of participants, respectively. The prevalence of prolonged P wave duration was 22.9%, 23.9%, and 24.3% in ≥30, 20–29, and <20 vitamin D category, respectively. And the prevalence of prolonged PR interval was 6.6%, 6.7%, and 7.5% in ≥30, 20–29, and <20 vitamin D category, respectively.

Using multivariable logistic regression analysis, in a model adjusted for all potential confounders, there was a statistically significant association between vitamin D deficiency and prolonged P wave duration (OR [95% CI]: 1.22 [1.03–1.45], p = 0.02; Table 2). There was also a significant association between vitamin D deficiency and prolonged PR interval in a fully adjusted model (OR [95% CI]: 1.48 [1.12–1.97], p = 0.006; Table 3).

Using P duration as a continuous outcome variable, in a multivariable linear regression analysis, 25(OH)D of <20 ng/ml was associated with longer P wave duration (β [95% CI]: 1.19 [0.33–2.05], p = 0.006) in the fully adjusted model (Table 2). 25(OH)D < 20 ng/ml was also associated with longer PR interval (β [95% CI]: 2.60 [1.87–4.33], p = 0.003) in fully adjusted model (Table 3).

We also calculated least mean square and standard error of P wave duration and PR interval across vitamin D categories using multivariable linear regression analysis (Supporting Information Table S1). Participants with 25(OH)D of <20 ng/ml had longer P wave duration and PR interval followed by those with 25(OH)D of 20–29 ng/ml and then 25(OH)D of ≥30 ng/ml.

Using multivariable logistic regression analysis, the association of 25(OH)D categories with prolonged P wave duration and prolonged PR interval was consistent across subgroups stratified by age, sex, and race (Table 4).

4 | DISCUSSION

In this large community-based population of adults without clinical CVD, there was a significant inverse association between vitamin D deficiency and LA abnormalities as measured by prolonged P wave duration and prolonged PR interval. These findings were consistent when P wave duration and PR interval were examined as categorical variables or continuous variables. The associations persisted despite adjustment for cardiovascular risk factor and other potential confounders. To our knowledge, this is the first study looking at the association of vitamin D levels and LA abnormalities.

Earlier studies examining the usefulness of P wave morphology in predicting CVD outcomes focused on AF (Holmqvist et al., 2010). However, later studies have also found that these P wave derived markers are predictive of stroke, sudden cardiac death, and all-cause mortality (Cheng et al., 2009; He et al., 2017; Magnani, Gorodeski et al., 2011; Montalvo et al., 2017), highlighting the potential role of these markers in predicting adverse outcome beyond AF. Our results showing that vitamin D is associated with increased risk of LA abnormalities may not only explain the mechanism by which vitamin D deficiency increases CVD but raise the possibility that vitamin D supplementation could improve LA abnormalities. However, that later assertion requires further investigation in a clinical trial.

Our study found that vitamin D deficiency was associated with both prolonged P wave duration and prolonged PR interval. P wave duration and PR interval used as AF predictors are readily measured from a standard 12-lead ECG and have shown good predictive accuracy for future AF, including paroxysmal AF (Andrikopoulos et al., 2000; Dilaveris et al., 1998; Materazzo, Piotti, Mantovani, Miceli, & Villani, 2007; Raitt, Kusumoto, Giraud,

TABLE 1 Baseline characteristics of study participants

Characteristics	Vitamin D ≥30 ng/ml	Vitamin D 20–29 ng/ml	Vitamin D <20 ng/ml	
Mean ± *SD* or *n* (%)	*n* = 1,873	*n* = 2,111	*n* = 1,910	*p*-Value[†]
Age (years)	59.1 ± 12.8	58.3 ± 13.0	56.5 ± 12.8	<0.0001
Male (%)	1,030 (54.9%)	962 (45.5%)	674 (35.2%)	<0.0001
Race				
Non-Hispanic White	1,293 (69.0%)	1,091 (51.6%)	554 (29.0%)	<0.0001
Non-Hispanic Black	166 (8.8%)	397 (18.8%)	733 (38.3%)	
Mexican American	346 (18.4%)	526 (24.9%)	539 (28.2%)	
Other	68 (3.6%)	97 (4.5%)	84 (4.4%)	
Total annual family income <20,000	720 (38.9%)	931 (44.9%)	903 (48.3%)	<0.0001
Systolic blood pressure (mmHg)	130.1 ± 18.6	131.0 ± 18.5	131.5 ± 19.6	0.05
Diastolic blood pressure (mmHg)	76.2 ± 9.6	76.1 ± 10.0	76.6 ± 10.2	0.26
Antihypertensive medications (%)	366 (19.5%)	403 (19.0%)	384 (20.1%)	0.72
Alcohol use (%) (current and former)	1,547 (83.8%)	1,684 (81.0%)	1,504 (80.7%)	0.02
Insulin resistance (%)	654 (34.9%)	845 (40.0%)	803 (42.1%)	<0.0001
Total cholesterol (mg/dl)	218.7 ± 42.1	217.9 ± 43.3	215.6 ± 44.6	0.06
Serum creatinine (mg/dl)	1.1 ± 0.3	1.1 ± 0.4	1.1 ± 0.4	<0.0001
Serum phosphorus (mg/dl)	3.38 ± 0.48	3.43 ± 0.49	3.44 ± 0.53	0.0002
eGFR (ml min^{-1} 1.73 m^{-2})[a]	68.5 ± 15.0	72.7 ± 18.7	77.0 ± 19.3	<0.0001
ACR (mg/g)[b]	6.2 (3.7–11.8)	6.5 (3.7–13.4)	7.2 (3.9–16.4)	<0.0001
C-reactive protein (mg/dl)	0.45 ± 0.80	0.46 ± 0.66	0.54 ± 0.78	0.0001
Body mass index (kg/m^2)	26.6 ± 4.6	27.6 ± 5.2	28.6 ± 6.3	<0.0001
Smoking (%)				
Current smoker	366 (19.5%)	454 (21.5%)	545 (28.5%)	<0.0001
Former smoker	705 (37.6%)	628 (29.7%)	509 (26.6%)	<0.0001
Never smoker	802 (42.8%)	1,029 (48.7%)	856 (44.8%)	0.0006
Physical activity (METs per week)[b]	16.7 (3.9–37.0)	10.4 (1.6–31.3)	4.6 (0–22.3)	<0.0001
Prolonged P wave duration	429 (22.9%)	505 (23.9%)	465 (24.3%)	0.56
Prolonged PR interval	124 (6.6%)	142 (6.7%)	144 (7.5%)	0.47
P wave duration (ms)	111.05 ± 13.03	111.52 ± 12.96	111.79 ± 13.05	0.20
PR interval (ms)	161.83 ± 25.22	162.35 ± 25.22	162.73 ± 25.90	0.54

Note. Insulin resistance defined as fasting blood glucose ≥100 mg/dl, or history of diabetes or taking medications. Current and former alcohol use defined as having at least 12 drinks in life.
ACR: Albumin/creatinine ratio; eGFR: estimated glomerular filtration rate; HDL: high-density cholesterol; MET: metabolic equivalent.
[a]GFR calculated from Modification of Diet in Renal Disease formula. [b]ACR and METs reported as median and IQR. [†]*p*-Value as calculated by ANOVA for continuous and chi-square for categorical variables.

TABLE 2 Association between vitamin D categories and P wave duration

Logistic regression models[a]						
	Model 1		Model 2		Model 3	
Vitamin D categories	Odds ratio (95% CI)	*p*-Value	Odds ratio (95% CI)	*p*-Value	Odds ratio (95% CI)	*p*-Value
Vitamin D ≥30 ng/ml	Reference		Reference		Reference	
Vitamin D 20–29 ng/ml	1.16 (0.99–1.35)	0.05	1.09 (0.93 to 1.27)	0.25	1.10 (0.94 to 1.29)	0.21
Vitamin D <20 ng/ml	1.35 (1.14–1.58)	0.001	1.20 (1.02 to 1.42)	0.04	1.22 (1.03 to 1.45)	0.02
Linear regression models[b]						
	Model 1		Model 2		Model 3	
	Beta-coefficient (95% CI)	*p*-Value	Beta-coefficient (95% CI)	*p*-Value	Beta-coefficient (95% CI)	*p*-Value
Vitamin D ≥30 ng/ml	Reference		Reference		Reference	
Vitamin D 20–29 ng/ml	1.00 (0.20–1.80)	0.01	0.58 (−0.20 to 1.38)	0.14	0.61 (−0.18 to 1.41)	0.12
Vitamin D <20 ng/ml	2.03 (1.19–2.88)	<0.0001	1.25 (0.40 to 2.11)	0.003	1.19 (0.33 to 2.05)	0.006

Note. Model 1 adjusted for age, sex, race, and socioeconomic status.
Model 2 adjusted for model 1 plus smoking and physical activity, BMI, and alcohol use.
Model 3 adjusted for systolic blood pressure, diastolic blood pressure, antihypertensive medications, insulin resistance, total cholesterol, CRP, serum phosphorus, eGFR, and urine albumin/creatinine ratio.
eGFR: estimated glomerular filtration rate.
[a]Odds ratio and 95% CI calculated using multivariable regression analysis. [b]Beta-coefficient and 95% CI calculated using multivariable linear regression analysis.

TABLE 3 Association between vitamin D categories and PR interval

Logistic regression models[a]						
	Model 1		Model 2		Model 3	
Vitamin D categories	Odds ratio (95% CI)	*p*-Value	Odds ratio (95% CI)	*p*-Value	Odds ratio (95% CI)	*p*-Value
Vitamin D ≥30 ng/ml	Reference		Reference		Reference	
Vitamin D 20–29 ng/ml	1.17 (0.91–1.52)	0.21	1.13 (0.87 to 1.47)	0.33	1.15 (0.88 to 1.51)	0.27
Vitamin D <20 ng/ml	1.61 (1.23–2.10)	0.0005	1.52 (1.15 to 2.01)	0.002	1.48 (1.12 to 1.97)	0.006
Linear regression models[b]						
	Model 1		Model 2		Model 3	
	Beta-coefficient (95% CI)	*p*-Value	Beta-coefficient (95% CI)	*p*-Value	Beta-coefficient (95% CI)	*p*-Value
Vitamin D ≥30 ng/ml	Reference		Reference		Reference	
Vitamin D 20–29 ng/ml	1.74 (0.16–3.32)	0.03	1.27 (−0.31 to 2.85)	0.11	1.42 (−0.17 to 3.02)	0.08
Vitamin D <20 ng/ml	3.73 (2.06–5.41)	<0.0001	2.65 (0.95 to 4.35)	0.002	2.60 (1.87 to 4.33)	0.003

Note. Model 1 adjusted for age, sex, race, and socioeconomic status.
Model 2 adjusted for model 1 plus smoking and physical activity, BMI, and alcohol (ever vs. never).
Model 3 adjusted for systolic blood pressure, diastolic blood pressure, antihypertensive medications, insulin resistance, total cholesterol, CRP, serum phosphorus, eGFR, and urine albumin/creatinine ratio.
eGFR: estimated glomerular filtration rate.
[a]Odds ratio and 95% CI calculated using multivariable regression analysis. [b]Beta-coefficient and 95% CI calculated using multivariable linear regression analysis.

& McAnulty, 2004). Several studies have examined the predictive value of these P wave morphology. Soliman, Prineas, Case, Zhang, and Goff (2009) studied 15,429 participants of ARIC cohort and found that P wave terminal force, maximum P wave duration, maximum P wave area, and PR interval used as AF predictors are strongly associated with the risk of incident AF. The study from FHS cohort by Magnani, Johnson et al. (2011) suggested that maximum P wave duration was significantly associated with AF.

TABLE 4 Association between vitamin D categories and (a) Prolonged P wave duration in subgroups, (b) Prolonged PR interval in subgroups

	Vitamin D categories	Odds ratio (95% CI)	Interaction *p*-value
(a)			
Male	Vitamin D 20–29 ng/ml	1.14 (0.92–1.41)	0.50
	Vitamin D <20 ng/ml	1.38 (1.05–1.71)	
Female	Vitamin D 20–29 ng/ml	1.05 (0.82–1.34)	
	Vitamin D <20 ng/ml	1.12 (0.87–1.45)	
Whites	Vitamin D 20–29 ng/ml	1.22 (0.99–1.50)	0.26
	Vitamin D <20 ng/ml	1.26 (0.97–1.64)	
Nonwhites	Vitamin D 20–29 ng/ml	0.95 (0.73–1.23)	
	Vitamin D <20 ng/ml	1.06 (0.82–1.36)	
Age >65 years	Vitamin D 20–29 ng/ml	1.19 (0.92–1.55)	0.47
	Vitamin D <20 ng/ml	1.28 (0.95–1.72)	
Age ≤65 years	Vitamin D 20–29 ng/ml	1.04 (0.85–1.28)	
	Vitamin D <20 ng/ml	1.17 (0.94–1.45)	
(b)			
Male	Vitamin D 20–29 ng/ml	1.13 (0.79–1.60)	0.89
	Vitamin D <20 ng/ml	1.63 (1.11–2.41)	
Female	Vitamin D 20–29 ng/ml	1.23 (0.81–1.87)	
	Vitamin D <20 ng/ml	1.43 (0.93–2.21)	
Whites	Vitamin D 20–29 ng/ml	1.00 (0.72–1.38)	0.38
	Vitamin D <20 ng/ml	1.20 (0.80–1.79)	
Nonwhites	Vitamin D 20–29 ng/ml	1.51 (0.91–2.50)	
	Vitamin D <20 ng/ml	1.78 (1.09–2.91)	
Age >65 years	Vitamin D 20–29 ng/ml	0.80 (0.55–1.17)	0.09
	Vitamin D <20 ng/ml	1.30 (0.86–1.97)	
Age ≤65 years	Vitamin D 20–29 ng/ml	1.71 (1.16–2.51)	
	Vitamin D <20 ng/ml	1.82 (1.21–2.73)	

Note. Odds ratio and 95% CI calculated using multivariable logistic regression analysis. Reference group = vitamin D ≥ 30 ng/ml. Model adjusted for age, sex, race, socioeconomic status, smoking and physical activity, BMI, alcohol, insulin resistance, systolic blood pressure, diastolic blood pressure, antihypertensive medications, total cholesterol, C-reactive protein, serum phosphorus, eGFR, and urine albumin/creatinine ratio.
eGFR: estimated glomerular filtration rate.

Similarly, the results from Copenhagen ECG study found both short and long P wave duration as well as longer PR intervals to be robustly associated with an increased risk of AF (Nielsen et al., 2015, 2013). These studies reveal the importance of LA abnormalities as measured by prolonged P wave duration and prolonged PR interval as risk predictors of AF.

There are several potential mechanisms by which vitamin D deficiency can lead to LA abnormalities. Vitamin D deficiency can cause activation of the renin–angiotensin–aldosterone system which is associated with atrial fibrosis and atrial dilatation (Demir, Uyan, & Melek, 2014; Li et al., 2002). Inflammation plays an important role in the development of atrial electrical and structural remodeling, and vitamin D deficiency has been linked to an increase in markers of inflammation (Barassi et al., 2012; Shea et al., 2008). Moreover, vitamin D deficiency can lead to increased parathyroid hormone level leading to intracellular calcium overload which has been linked to remodeling in atria (De Jong et al., 2011). These structural and electrical remodelings of atria can cause atrial dilatation and increased atrial conduction time, which may ultimately lead to prolonged P wave duration and prolonged PR interval. Given the prior reports linking prolonged P wave duration and PR interval to AF (Cheng et al., 2009; Magnani, Johnson et al., 2011) and given our results, it could be speculated that the impact on LA abnormalities could be one of these multifaceted factors. The exact mechanisms linking vitamin D deficiency and LA abnormalities should be an area of future research.

The strength of our study includes its large sample size, community-based and multiracial population, and better generalizability of the US population. Also, we were able to adjust for many potential confounders and mediators including lifestyle variables and CVD risk factors. Our study has certain limitations that need to be taken into consideration. First, our study design was cross-sectional, and

therefore, a causal relationship between vitamin D with P wave duration and PR interval could not be established. Second, we had only a single measurement of 25(OH)D that may not reflect long-term vitamin D status. Unfortunately, some of the measurements like smoking and physical activity are self-reported and thus subjected to recall bias. Finally, we adjusted for several confounders, but residual confounding remains a possibility.

5 | CONCLUSION

Our study has shown that vitamin D deficiency is associated with the predictors of AF. These results may provide evidence of the possible mechanism by which vitamin D deficiency increases the risk of CVD. Future studies should explore the possible pathophysiological basis for the association of vitamin D deficiency with P wave duration and PR interval, and whether vitamin D supplementation improves LA abnormalities.

CONFLICT OF INTEREST

None.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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