Published in final edited form as:

Am J Cardiol. 2013 February 1; 111(3): 418–424. doi:10.1016/j.amjcard.2012.10.021.

Relation of Vitamin D and Parathyroid Hormone to Cardiac Biomarkers and to Left Ventricular Mass (From the Cardiovascular Health Study)

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Abstract

Vitamin D and parathyroid hormone (PTH) may impact cardiovascular health among individuals with kidney disease and in the general population. We investigated associations of serum 25-hydroxyvitamin D (25OHD) and PTH concentrations with a comprehensive set of biochemical, electrocardiographic and echocardiographic measurements of cardiac structure and function in the Cardiovascular Health Study. A total of 2,312 subjects who were free of cardiovascular disease at baseline were studied. Serum 25OHD and intact PTH concentrations were measured using mass-spectrometry and a 2-site immunoassay. Outcomes were N-terminal pro-B-type natriuretic peptide (NT-proBNP), cardiac troponin T, electrocardiographic measures of conduction, and echocardiographic measures of left ventricular mass and diastolic dysfunction. At baseline, subjects had a mean age of 73.9±4.9 years, 69.7% were female and 21% had chronic kidney disease (CKD; glomerular filtration rate <60ml/min). Mean (SD) 25OHD was 25.2 (10.2) ng/ml and median PTH was 51 pg/ml (range 39–65 pg/ml). After adjustment, 25OHD was not associated with any of the biochemical, conduction, or echocardiographic outcomes. Serum PTH levels 65 pg/ml were associated with greater NT-proBNP, cardiac troponin T and left ventricular mass in subjects with CKD. The regression coefficients were: 120 (36.1, 204 pg/ml), 5.2 (3.0, 7.4 pg/ml) and 17 (6.2, 27.8 g) (p-value <0.001). In subjects with normal kidney function, PTH was not associated with the outcomes. Among older adults with CKD, PTH excess is associated with higher NT-pro-BNP, cardiac troponin T, and left ventricular mass. In conclusion, these findings suggest a role for PTH in cardiovascular health and the prevention of cardiac diseases.

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Conflict of interest

None declared

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Keywords

Vitamin D; parathyroid hormone; cardiac biomarkers; left ventricular mass; epi-demiology

Introduction

Insufficient vitamin D and excess of parathyroid hormone (PTH), beyond their effects on calcium homeostasis and bone mineralization, are associated with higher risk of cardiovascular diseases (1–3). The LURIC study, a large cohort of patients referred for angiography showed an independent association between 25OHD and an up-regulated circulating renin-angiotensin system (4). This implies that 25OHD might have antihypertensive and tissue-protective properties attributed to the inhibition of renin synthesis. We previously measured serum 25OHD and PTH levels in 2,312 subjects from the Cardiovascular Health Study (CHS) who were free of clinical cardiovascular disease (2). In this community-based sample, lower serum 25OHD levels were associated with incident myocardial infarction and higher PTH levels were associated with incident heart failure during 14 years of follow-up. Given these associations with cardiovascular events, we investigate relations of 25OHD and PTH with biochemical, electrocardiographic and structural measurements of cardiac function.

Methods

The Cardiovascular Health Study (CHS) is a prospective, community-based, multicenter cohort study of determinants of cardiovascular risk and prognosis among older adults (5). In 1989 and 1990, the CHS enrolled 5,201 ambulatory men and women age 65 years and older from Medicare eligibility lists in Forsyth County, NC (latitude north 36°6′); Sacramento County, CA (38°35′); Washington County, MD (39°38′); and Pittsburgh, PA (40°27′). The CHS enrolled an additional 687 African American subjects in 1992 and 1993. The investigation conforms with the principles outlined in the Declaration of Helsinki. Each center's institutional review committee approved the study and all subjects gave written informed consent.

For analyses of cardiac biomarkers we evaluated the sample of 2,312 CHS subjects who were free of clinical cardiovascular disease at the time of their 1992–1993 examination and had available serum measurements of 25OHD, PTH and cardiac biomarkers (2). For analyses of electrocardiographic measurements we further excluded 22 subjects who did not complete an electrocardiogram (ECG) at their 1992–1993 study visit, which resulted in 2290 subjects with ECG conduction measurements.

Between the 1992–1993 and 1994–1995 CHS exams, 96 subjects died. An additional 300 subjects did not complete echocardiography measurements as part of the 1994–1995 examination and an additional 495 did not complete echocardiographic measurements to calculate LV mass. Final sample sizes for Doppler and LV mass measurements were 1,575 and 1,399 respectively. Subjects who did not complete electrocardiographic and echocardiographic measurements were older (74.8 years vs. 73.4 years) and more likely to be male (37% vs. 25%).

All measurements were performed on serum samples stored at –70°C and thawed just before testing (maximum of 3 freeze-thaw cycles) (6). The University of Washington Clinical Nutrition Research Unit performed total 25OHD measurements from serum collected during the 1992–1993 CHS exams using high-performance liquid chromatography and tandem mass spectrometry on a Waters Quattro micro mass spectrometer (Waters, Milford, Massachusetts). The inter-assay coefficient of variation was <3.4%. Intact serum PTH was

quantified using a 2-site immunoassay on a Beckman UniCel DxI clinical analyzer (Beckman Coulter, Brea, California). The inter-assay coefficient of variation for PTH was 4.5% at 37 pg/mL. Serum non-ionized total calcium levels were measured using indirect potentiometry. Serum phosphorus levels were measured using a timed-rate colorimetric reaction method with ammonium molybdate on a Beckman DxC Synchron analyzer (Beckman Coulter).

Serum N-terminal pro-B-type natriuretic peptide (NT-proBNP) was measured in 2008 and cardiac troponin T (cTnT) was measured in 2010 on the Elecsys 2010 system (Roche Diagnostics, Indianapolis, Indiana) expressed in pg/mL. Serum cTnT concentrations were measured with highly sensitive cTnT reagents and the analytical measurement range was 3 to 10 000 pg/mL (7). The coefficient of variation for the NT-proBNP inter-assay was 2% to 5% during the testing period, and the analytical measurement range for was 5 to 35,000 pg/ml (8).

A standardized resting 12-lead ECG was recorded in the supine position, and processed using the Marquette 12SL ECG analysis program (GEMS-IT, Milwaukee, Wisconsin), which clusters QRS-T complexes from a ten second recording of eight independent simultaneous ECG leads (9).

Echocardiographic images were obtained using a standardized protocol and recorded onto super VHS tape with a Toshiba SSH-160A cardiac ultrasound machine (10). The core reading center for the echocardiograms was located at Georgetown University, Washington, DC. The methods for 2-dimensional, Doppler, and M-mode transthoracic echocardiography in the CHS have been previously described (10). Data were evaluated at a centralized echocardiography center by readers blinded to the subjects' clinical information. Quality control measures included standardized training of echocardiography for technicians and readers, observation of technicians by a trained echocardiographer and periodic blind duplicate readings (10).

LV mass was estimated using M-mode echocardiography. The LV outflow tract velocity–time integral and diastolic flow measures, such as mitral early (E) and late (A) wave peak velocities, were assessed using 2-dimensional directed Doppler echocardiography. Fractional shortening at the endocardium and midwall was calculated from M-mode measurements.

Trained CHS study personnel conducted standardized interviews at the 1992–1993 visit, which queried demographics, health status, smoking status, and alcohol use (5). CHS study personnel assessed prescription and over-the-counter medication use, including vitamin D supplements, by instructing subjects to bring in all of their medications and directly transcribing the medication bottle labels. Blood pressure was measured in triplicate 5 min apart with the participant seated and performed phlebotomy under fasting conditions. Diabetes was defined as a fasting glucose level 7.0 mmol/l or the use of insulin or an oral hypoglycemic medication. Hypertension was categorized as present if seated systolic blood pressure was 140 mmHg or higher, or diastolic blood pressure was 90 mmHg or higher, or the patient self-reported a history of hypertension in combination with use of antihypertensive medication. The Laboratory for Clinical Biochemistry Research analyzed blood specimens for albumin, total and high-density lipoprotein cholesterol, creatinine, and C-reactive protein levels (5). We calculated estimated glomerular filtration rate (GFR) according to the Chronic Kidney Disease – Epidemiology formula. We defined chronic kidney disease (CKD) as GFR <60ml/min.

We analyzed 25OHD concentrations according to previously published categories used in CHS: >30 ng/mL, 15 < 30 ng/mL, < 15 ng/mL (2). Serum 25(OH)D concentration was

categorized using a threshold of 15 ng/ml, because 25(OH)D concentrations below this level are associated with increased risk for incident cardiovascular events (2, 3).

We examined serum PTH concentrations dichotomously as <65 pg/ml versus ≥65 pg/ml, because functional analyses revealed threshold associations of serum PTH levels ≥65 pg/ml with study outcomes. We defined primary hyperparathyroidism as a serum PTH levels ≥65 pg/ml plus a serum calcium level >10.2 mg/dl, as previously published (11).

We constructed linear regression models to estimate regression coefficients for associations of 25OHD and PTH with biochemical, electrocardiographic and echocardiographic measurements after adjustment for potential confounding variables. A basic model included 25OHD or PTH as exposure variable and was adjusted for age, race, sex, season of the year, clinic site, height and weight. A second model included established cardiovascular risk factors: diabetes type 2, smoking, education, physical activity, systolic blood pressure, anti-hypertensive medication and C-reactive protein. In the case of PTH, model 2 was also adjusted for total 25OHD, because vitamin D deficiency is a known risk factor for hyperparathyroidism. A third model added estimated GFR to describe separately the influence of adjustment for kidney function.

We used the likelihood ratio test to investigate potential interactions of CKD status on associations of 25OHD and PTH with study outcomes. For statistically significant interactions we present separate results for subjects who have and do not have CKD. All reported intervals are 95% confidence intervals, and all p-values are two-sided. We conducted analyses using SPSS version 19.0 (SPSS Inc., Chicago, Illinois).

Results

At baseline, subjects had a mean age of 74±4.9 years, 70% were female and 21% had CKD. Mean serum 25OHD was 25±10. ng/ml. The prevalence of vitamin D deficiency (<15 ng/ml) was 17% and insufficiency (15 to 30 ng/ml) was 54%. Lower serum 25OHD concentrations were related to African American race, female sex, measurement during winter months, prevalent diabetes, current smoking, higher body mass index, lesser physical activity, higher systolic blood pressure, and higher serum CRP levels (Table 1).

Serum PTH levels showed a distribution skewed to the right, with a median value of 51 pg/ml (interquartile range 39 to 65 pg/ml). The proportion of subjects who had PTH levels ≥65 was 25%. Higher serum PTH concentrations were associated with African American race, female sex, higher systolic blood pressure, and lower estimated GFR. Serum phosphorus levels were slightly lower among subjects who had serum PTH levels ≥65 pg/ml. Serum 25OHD concentrations were inversely correlated with serum PTH concentrations, especially for values below 20 ng/ml of 25OHD.

In unadjusted analyses, lower serum 25OHD levels were associated with higher NT-proBNP concentrations but not with cTnT (Table 2). Associations of 25OHD with NT-proBNP were removed by adjustment for demographics and traditional cardiovascular risk factors. In contrast, higher serum PTH levels remained associated with both NT-proBNP and cTnT in demographic, cardiovascular risk factor and estimated GFR adjusted analyses. We detected a significant interaction of estimated kidney function on associations of PTH levels with cardiac biomarkers (p-interaction <0.001) with substantially stronger associations among subjects with CKD (Figure 1).

Neither 25OHD nor PTH levels were associated with electrocardiographic measures of atrioventricular or ventricular conduction (Table 3). Adjustment for demographic characteristics did not alter these negative findings. There was no significant effect

modification by estimated kidney function ($P > 0.115$) on associations of 25OHD and PTH and the electrocardiographic markers.

Lower serum 25OHD levels were associated with a lower E/A ratio, a measure of diastolic function, in unadjusted analyses (Table 4). This association disappeared after adjusting for basic confounders. Serum 25OHD levels were not associated with LV mass or fractional shortening.

Higher PTH levels were associated with greater LV mass, but not with E/A ratio or fractional shortening. After full adjustment, a serum PTH level ≥ 65 pg/mL was associated with a 6.1 (95% CI 1.0, 11.2) gram greater LV mass. Similar to the cardiac biomarkers, we detected a significant interaction of kidney function on the association of PTH with LV mass (interaction $p < 0.001$) and therefore we stratified analyses by kidney function (figure 1c).

None of the associations changed when we excluded subjects ($n=21$) who met the definition of primary hyperparathyroidism.

Discussion

In this community-based cohort of ambulatory older adults who were free of clinical cardiovascular disease, serum PTH concentrations were associated with greater NT-proBNP and cTnT concentrations and greater LV mass after adjustment for demographics, traditional cardiovascular risk factors and kidney function. Associations were strongest among subjects who had CKD. Lower 25OHD concentrations were not associated with any of the cardiac measurements studied.

This study demonstrates that higher PTH concentrations are associated with biochemical evidence of cardiac deterioration in a general population free of cardiovascular diseases. The biochemical marker NT-proBNP serves as a sensitive marker for early cardiac deterioration and the marker cTnT serves as an indicator of cardiomyocyte necrosis (12). Higher PTH was also associated with higher LV mass in subjects with CKD which is a measure of cardiac structure. Serum PTH was not associated with electrocardiographic measures, fractional shortening and E/A ratio. This suggests that it is more likely that PTH is involved in hypertrophic cell growth and myocardial stretch than to cardiac output and diastolic function (13).

Among patients with end-stage renal disease and among patients with primary hyperparathyroidism there are historical associations of PTH excess with hypertension and LV mass (14, 15). In patients with primary hyperparathyroidism, parathyroidectomy improved some cardiovascular disorders like LV hypertrophy, impaired glucose metabolism and dyslipidemia, although, surgery had little effect on the prevalence of hypertension (16, 17). Consistent with our results, PTH was associated with LV mass in middle age men and women in Norway, although they did not adjust for kidney function nor examine the interaction with CKD, which might have influenced the results (13). In a smaller study in an older Dutch population, PTH was associated with LV mass in individuals with lower GFR after 8 years of follow-up (18). Studies conducted in patient settings such as end stage renal disease, primary hyperparathyroidism, subjects undergoing angiography showed inconsistent results between PTH and cardiovascular events and other cardiac measures (19–23). Also, in adolescents, PTH was not associated with cardiovascular risk factors (24). Differences in age, disease history and length of follow-up, may explain the differences between the risk estimates.

There are potential mechanisms through which high PTH could harm the cardiac system. Serum PTH excess may represent inadequate biologic vitamin D activity because it responds

directly to calcitriol, the activated form of vitamin D (25). In a feedback loop, PTH enhances calcitriol production by the kidneys; however substrate 25OHD levels are not altered. Also, PTH receptors have been demonstrated in the heart and exert a trophic effect on cardiomyocytes (26). Furthermore, PTH activates protein kinase C which could lead to hypertrophic growth and expression of fetal type proteins in cardiomyocytes (26). This hypertrophic effect of PTH might contribute to biochemical changes and higher LV mass and incident heart failure (2, 13, 27).

Parathyroid hormone could also be a marker of duration of kidney damage while simultaneously exerting direct deleterious effects on cardiac structure and function. The compensatory mechanism of PTH to maintain calcium and phosphorus levels within physiological ranges despite renal phosphate retention and decreasing 1,25 dihydroxyvitamin D production could be a first signal of complications related to CKD (25). In contrast, it could also be the other way around: a decline in kidney function represented by higher PTH levels could contribute directly to cardiac pathology by diverse mechanisms such as contractile performance, myocardial calcification, fibrosis, and hypertrophy (26, 27). This might be an explanation for the observed interaction for PTH and the cardiac measures by GFR group. The relationship between GFR and incident CHF seems to be non-linear (28), we therefore tested also GFR as a categorical variable (<60, 60–90, >90 ml/min), however it did not change the results.

This study has several important strengths, which include a generally healthy, community-based study population that was free of baseline clinical cardiovascular disease and a larger sample size compared to previous studies (13, 29). Furthermore we used standardized methods to assess 25OHD and PTH, biochemical and structural cardiac measures, cardiovascular risk factors, kidney function, and other covariates. Associations of 25OHD and PTH in relation to cardiac biomarkers, electrocardiographic, echocardiographic measurements have not been studied extensively. This study represents a relevant step forward toward unraveling the potential role of 25OHD and PTH in the pathophysiology of cardiac diseases.

The selection of a cardiovascular disease free population may have limited generalizability to populations with cardiac diseases and may have reduced study power. The cross-sectional design is unable to distinguish the temporal sequence between PTH excess and cardiac biomarkers or echocardiographic findings. Higher serum PTH concentrations were associated with higher systolic blood pressure, and lower estimated GFR, so it could be that PTH is a marker of other abnormalities along the same pathway such as vitamin D deficiency or CKD that predispose to a cardiac deterioration. We adjusted for these factors, however, the interplay between the circulating concentrations of PTH, vitamin D, and kidney function is complex. Moreover, previous research indicated that serum 25OHD is independently associated to the renin-angiotensin system(4) and serum PTH increased the secretion of aldosterone levels (30). In the current study we have not data on renin or aldosterone. Future studies would benefit measuring these factors to investigate the impact of these potential interactions on 25OHD and PTH in relation to cardiac measures.

This study showed that high PTH concentrations were associated with greater cardiac biomarkers and LV mass in subjects with CKD. Because the presence of cardiac diseases is independently associated with kidney function decline, it appears that the relationship between CKD and cardiac deterioration is bidirectional. However, our results suggest that PTH excess is only associated with cardiac measures in subjects with CKD. The presence of even mild renal insufficiency is a condition that should be taken into account for the prevention of cardiovascular disease risk.

Acknowledgments

List of support/grant information: This work was supported by contracts N01-HC-85239, N01-HC-85079 through N01-HC-85086, N01-HC-35129, N01 HC-15103, N01 HC-55222, N01-HC-75150, N01-HC-45133, and grant HL080295 from the National Heart, Lung, and Blood Institute (NHLBI), with additional contribution from the National Institute of Neurological Disorders and Stroke (NINDS). Additional support was provided through AG-023629, AG-15928, AG-20098, and AG-027058 from the National Institute on Aging (NIA).

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Figure 1.

abc: Regression coefficients for PTH with cardiac biomarkers and LV mass by CKD group

P-for interaction for NT-proBNP, cTnT and LV mass with GFR: <0.003

Adjusted for age, race, sex, season of the year, clinic site, height, weight, type 2 diabetes, kilocalories of physical activity, education, smoking status, ant-hypertensive medication, systolic blood pressure, C-reactive protein, vitamin D and GFR

Table 1
Participant characteristics by 25-hydroxyvitamin D and parathyroid hormone concentrations

Variable	Serum 25OHD (ng/mL)			Serum PTH (pg/mL)		
	>30	15–30	<15	<65	65	
Number of participants	681 (29%)	1247 (54%)	384 (17%)	1742 (75%)	570 (25%)	
Age (years)	73±4	74±5	74±6	74±5	75±6	
Females (%)	394 (58%)	912 (73%)	305 (79%)	1187 (68%)	424 (74%)	
African American (%)	30 (4%)	160 (13%)	142 (37%)	226 (13)	107(19)	
Season						
Winter	112 (16%)	303 (24%)	169 (44%)	413 (24%)	171 (30%)	
Spring	109 (16%)	302 (24%)	118 (31%)	386 (22%)	143 (25%)	
Summer	286 (42%)	339 (27%)	45 (12%)	538 (31%)	132 (23%)	
Autumn	174 (26%)	303 (25%)	52 (13%)	405 (23%)	124 (22%)	
Study site						
Forsyth County, North Carolina	195 (29%)	387 (31%)	103 (27%)	513 (30%)	172 (30%)	
Sacramento County, California	199 (29%)	264 (21%)	94 (24%)	390 (22%)	167(29%)	
Washington County, Maryland	152 (22%)	334 (27%)	76 (20%)	449 (26%)	113 (20%)	
Pittsburgh, Pennsylvania	135 (20%)	262 (21%)	111 (29%)	390 (22%)	118 (21%)	
Education level						
Low	73 (11%)	207 (17%)	87 (23%)	262 (15%)	105 (18%)	
Intermediate	256 (38)	469 (38%)	145 (38%)	654 (38%)	216 (38%)	
High	349 (51%)	569 (45%)	151 (39%)	823 (47%)	246 (44%)	
Type 2 diabetes (%)	55 (8%)	134 (11%)	76 (20%)	196 (11%)	69 (12%)	
Cigarette smokers (%)	54 (8%)	116 (10%)	58 (16%)	180 (10%)	48 (9%)	
Physical activity (kcal/week)	2479±2421	1772±1911	1243±1676	1964±2111	1672±1978	
Body mass index (kg/m ²)	25.5±3.9	27.1±4.8	27.9±5.5	26.4±4.5	27.8±5.4	
Systolic blood pressure (mmHg)	132±20	135±21	139±21	133±20	139±23	
Diastolic blood pressure (mmHg)	70±11	71±11	72±11	70±11	73±12	
Serum measurements						
25OHD (ng/mL)	37±8	23±4	11±3	27±10	21±9	
PTH (pg/ml)	49±27	57±26	71±39	44±12	94±37	

Variable	Serum 25OHD (ng/mL)			Serum PTH (pg/mL)	
	>30	15–30	<15	<65	65
Calcium (mg/dl)	9.5±0.3	9.5±0.4	9.5±0.4	9.5±0.4	9.5±0.4
Phosphorus (mg/dl)	3.6±0.5	3.6±0.5	3.6±0.5	3.6±0.5	3.5±0.5
Total cholesterol (mg/dl)	210±37	211±35	212±39	210±36	214±39
HDL cholesterol (mg/dl)	57±16	55±14	56±14	56±15	54±14
Estimated GFR (ml/min/1.73 m ²)	71±15	74±16	74±17	74±15	69±18
GFR <60 mL/min/1.73m ² (%)	146 (21%)	210 (17%)	65 (17%)	317 (18%)	174 (31%)
Triglycerides (mg/dl)	132±71.1	137±68.8	130±64.2	132±66.5	140±75.0
C-reactive protein (mg/l)	3.6±6.9	4.1±7.4	5.7±10.1	4.1±7.9	4.5±7.4
Medication use					
Any antihypertensive agent	252 (37%)	486 (39%)	187 (49%)	663 (38%)	262 (46%)
Thiazide diuretic agent	56 (8%)	131 (11%)	53 (14%)	183 (11%)	57 (10%)
Loop diuretic agent	15 (2%)	45 (4%)	16 (4%)	39 (2%)	37 (7%)
Vitamin D supplement	10 (1.5%)	0 (0%)	0 (0%)	8 (0.5)	2 (0.4)
Calcium supplement	7 (1.0%)	9 (0.7%)	2 (0.5%)	16 (0.9)	2 (0.4)

Values are mean±SD or N (%)

25OHD: 25-hydroxyvitamin D, PTH: parathyroid hormone, GFR: glomerular filtration rate, HDL: high density lipoprotein

Table 2
Associations of serum 25-hydroxyvitamin D and parathyroid hormone with cardiac biomarkers

	N	Mean value	Model 1	Model 2	Model 3
NT-proBNP (pg/mL)					
25OHD > 30 (ng/mL)	681	194±304	<i>Reference</i>	<i>Reference</i>	<i>Reference</i>
25OHD 15–30 (ng/mL)	1247	192±305	* –5.9 (–45.9, 34.1)	–17.2 (–77.5, 43.1)	–9.3 (–69.1, 50.6)
25OHD <15 (ng/mL)	384	273±783	67.2 (10.2, 124)	39.0 (–59.4, 137)	44.1 (–53.5, 142)
P-for trend		0.011	0.061	0.446	0.382
PTH <65 (pg/mL)	1742	186±391	<i>Reference</i>	<i>Reference</i>	<i>Reference</i>
PTH ≥65 (pg/mL)	570	267±509	56.1 (16.1, 96.1)	48.0 (7.4, 88.7)	31.7 (–9.0, 72.4)
P-value (pg/mL)		<0.001	0.006	0.021	0.127
cTnT (pg/mL)					
25OHD > 30 (ng/mL)	680	7.5±12.3	<i>Reference</i>	<i>Reference</i>	<i>Reference</i>
25OHD 15–30 (ng/mL)	1246	7.7±11.0	0.1 (–0.9, 1.2)	0.1 (–1.1, 1.1)	0.5 (–0.5, 1.6)
25OHD <15 (ng/mL)	384	8.1±9.9	0.3 (–1.2, 1.8)	–0.2 (–1.8, 1.3)	0.4 (–1.1, 1.9)
P-for trend		0.333	0.698	0.803	0.491
PTH <65 (pg/mL)	1740	7.0±8.1	<i>Reference</i>	<i>Reference</i>	<i>Reference</i>
PTH ≥65 (pg/mL)	570	9.8±17.5	2.3 (1.2, 3.3)	2.2 (1.1, 3.3)	1.6 (0.5, 2.6)
P-value		<0.001	<0.001	<0.001	0.004

NT-proBNP: N-terminal pro-B-type natriuretic peptide, 25OHD: 25-hydroxyvitamin D, PTH: parathyroid hormone, cTnT: Cardiac troponin T

* Values are regression coefficients in pg/mL with 95% confidence intervals

Model 1: adjusted for age, race, sex, season of the year, clinic site, height, and weight

Model 2: Model 1 + type 2 diabetes, kilocalories of physical activity, education, smoking status, anti-hypertensive medication, systolic blood pressure, C-reactive protein, vitamin D (in case of PTH models)

Model 3: Model 2 + estimated glomerular filtration rate creatinine (CKD-EPI formula)

Table 3

Association of serum 25-hydroxyvitamin D and parathyroid hormone with electrocardiographic measures of conduction

	N	Mean value	Model 1
<i>Atrioventricular conduction PR (ms)</i>			
25OHD > 30 (ng/mL)	679	170±29.4	<i>Reference</i>
25OHD 15–30 (ng/mL)	1240	171±29.2	*−1.2 (−1.6, 4.0)
25OHD <15 (ng/mL)	371	168±28.8	−1.9(−5.9, 2.1)
P-for trend		0.503	0.583
PTH <65 (pg/mL)	1727	170±29.0	<i>Reference</i>
PTH ≥65 (pg/mL)	563	171±29.6	−0.1 (−3.0, 2.7)
P-value		0.421	0.272
<i>Ventricular conduction QRS (ms)</i>			
25OHD > 30 (ng/mL)	679	91.9±15.8	<i>Reference</i>
25OHD 15–30 (ng/mL)	1240	91.4±16.8	0.4 (−1.2, 1.9)
25OHD <15 (ng/mL)	371	91.0±17.5	0.9 (−1.4, 3.1)
P-for trend		0.555	0.455
PTH <65 (pg/mL)	1727	91.4±16.3	<i>Reference</i>
PTH ≥65 (pg/mL)	563	91.9±17.6	0.5 (−1.1, 2.0)
P-value		0.534	0.563

25OHD: 25-hydroxyvitamin D, PTH: parathyroid hormone

* Values are regression coefficients in msec with 95% confidence intervals

Model 1: adjusted for age, race, sex, season of the year, clinic site, height, and weight

Table 4
Associations of serum 25-hydroxyvitamin D and parathyroid hormone with structural measures

LV mass (g) (echo)	N	Mean ± SD	Model 1	Model 2	Model 3
25 OHD > 30 (ng/mL)	430	145±42.4	Reference	Reference	Reference
25 OHD 15–30 (ng/mL)	746	144±44.7	−1.6 (−6.4, 3.2)	0.05 (−7.1, 7.2)	−0.4 (−7.6, 6.8)
25 OHD <15 (ng/mL)	223	140±49.0	−3.6 (−10.6, 3.3)	−1.5 (−13.3, 10.3)	−1.9 (−13.7, 9.9)
P-for trend		0.226	0.300	0.811	0.754
PTH <65 (pg/mL)	1067	142±41.3	Reference	Reference	Reference
PTH 65 (pg/mL)	332	150±53.8	4.6 (−0.3, 9.5)	5.2 (0.2, 10.3)	6.1 (1.0, 11.2)
P-value		0.003	0.068	0.043	0.019
Fractional shortening (%)					
25 OHD > 30 (ng/mL)	430	41.7±7.8	Reference	Reference	Reference
25 OHD 15–30 (ng/mL)	746	41.6±7.9	−0.2 (−1.2, 0.8)	−1.4 (−2.9, 0.1)	−1.4 (−2.9, 0.1)
25 OHD <15 (ng/mL)	223	42.6±7.7	0.4 (−1.0, 1.8)	−1.8 (−4.2, 0.6)	−1.8 (−4.2, 0.7)
P-for trend		0.253	0.745	0.144	0.149
PTH <65 (pg/mL)	1067	41.7±7.9	Reference	Reference	Reference
PTH 65 (pg/mL)	332	41.8±7.8	0.1 (−1.0, 1.1)	−0.1 (−1.2, 1.0)	−0.1 (−1.2, 0.9)
P-value		0.902	0.893	0.849	0.798
E/A ratio (Doppler)					
25 OHD > 30 (ng/mL)	517	0.92±0.27	Reference	Reference	Reference
25 OHD 15–30 (ng/mL)	855	0.88±0.32	−0.01 (−0.04, 0.02)	−0.01 (−0.06, 0.03)	−0.01 (−0.06, 0.03)
25 OHD <15 (ng/mL)	203	0.86±0.21	−0.02 (−0.06, 0.03)	−0.02 (−0.10, 0.06)	−0.02 (−0.10, 0.06)
P-for trend		0.002	0.423	0.607	0.600
PTH <65 (pg/mL)	1220	0.89±0.26	Reference	Reference	Reference
PTH 65 (pg/mL)	355	0.88±0.38	0.02 (−0.02, 0.05)	0.02 (−0.02, 0.05)	0.02 (−0.02, 0.05)
P-value		0.701	0.369	0.332	0.313

25OHD: 25-hydroxyvitamin D, PTH: parathyroid hormone

* Values are regression coefficients with 95% confidence intervals

LV: left ventricular, E/A ratio: early and late ventricular filling velocity

Model 1: adjusted for age, race, sex, season of the year, clinic site, height, and weight

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Model 2: Model 1 + type 2 diabetes, kilocalories of physical activity, education, smoking status, anti-hypertensive medication, systolic blood pressure, C-reactive protein, vitamin D (in case of PTH models)
Model 3: Model 2 + estimated glomerular filtration rate creatinine (CKD-EPI formula)