Plasma Parathyroid Hormone Level and Prevalent Cardiovascular Disease in CKD Stages 3 and 4: An Analysis From the Kidney Early Evaluation Program (KEEP)

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Background: Cardiovascular disease (CVD) is the most common cause of death in patients with chronic kidney disease (CKD). Secondary hyperparathyroidism is common in patients with CKD, and its relationship to CVD is not well defined. This analysis aims to assess whether serum intact parathyroid hormone (PTH) level is an independent risk factor for CVD in patients with CKD stages 3 and 4.

Methods: In this cross-sectional study, medical history surveys, including CVD events, were collected from 4,472 patients with stages 3 and 4 CKD identified by the National Kidney Foundation Kidney Early Evaluation Program (KEEP), which included blood pressure measurement and laboratory testing. Age, hemoglobin level, estimated glomerular filtration rate, serum phosphorus level, and serum calcium level were evaluated as continuous variables, and plasma PTH levels, by tertile: less than 35, 35 to 70, and greater than 70 pg/mL. Multivariate logistic regression was used to estimate odds ratios (ORs) of CVD predictor variables.

Results: Mean age was 68.3 ± 11.8 years. Of the study population, 68% were women, 69% were white, 6% were current smokers, 45% were obese, 46% had diabetes, and 83% had hypertension. A history of CVD was present for 1,972 (44.1%), and plasma PTH level greater than 70 pg/mL, for 2,239 (50.1%). Multivariate logistic regression showed ORs for CVD events increasing with age (OR, 1.03; $P < 0.001$), male sex (OR, 1.51; $P < 0.001$), diabetes (OR, 1.73; $P < 0.001$), hypertension (OR, 1.43; $P < 0.001$), and intact PTH level greater than 70 pg/mL (OR, 1.51; $P < 0.001$; reference, <35 pg/mL).

Conclusions: PTH level greater than 70 pg/mL is independently associated with CVD events in patients with CKD stages 3 and 4. No association was observed between serum phosphorus or calcium level and CVD events. These findings provide support for intact PTH testing, along with testing for other indicators of CKD mineral and bone disorders, at earlier CKD stages.

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INDEX WORDS: Cardiovascular disease; chronic kidney disease; parathyroid hormone.

Chronic kidney disease (CKD) is well established as a risk state that results in greater rates of prevalent and incident cardiovascular disease (CVD),[1-3] and CVD is the most common cause of death in patients with CKD. As estimated glomerular filtration rate (eGFR) decreases to less than 60 mL/min/1.73 m^2 in populations, CVD prevalence and future mortality increase.[4]

Increased attention has been focused on endocrine abnormalities in patients with advanced CKD to help explain these associations.[5,6] Mineral and bone disorders related to CKD are defined by abnormalities in phosphate retention, hypercalcemia or hypocalcemia, hyperparathyroidism, increased alkaline phosphatase level, abnormalities in bone turnover, and vascular and soft-tissue calcification.[7] Secondary hyperparathyroidism is often the first and most recognizable laboratory signal of this complication because parathyroid hormone (PTH) is a compensatory mechanism to maintain calcium and phosphorus levels within physiological ranges despite renal phosphate retention and decreasing 1,25 dihydroxyvitamin D production. Increased PTH levels predict myocardial and coronary heart disease in people with normal calcium levels and no kidney failure.[8] PTH has been linked to a plethora of adverse cardiovascular events,[9] and PTH receptors are present in the heart.[10] Increases in PTH levels are known to increase cardiac contrac-

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tility[11,12] and induce myocardial hypertrophy[13] and interstitial fibrosis[14] in animal studies. Clinical studies indicate that PTH may contribute to the development of left ventricular hypertrophy.[15] Increased PTH levels can exacerbate atherosclerosis by contributing to hyperlipidemia[16,17] and impaired glucose tolerance.[18,19] Effects of PTH on vascular endothelial function and growth may contribute to increased vascular tone and stiffness,[20-22] thereby leading to hypertension. PTH may have a role in the calcification of atherosclerotic lesions.[23,24]

Most data related to PTH and CVD outcomes are based on patients with stage 5 CKD who are on dialysis therapy and being treated with a variety of drugs that influence calcium, phosphorus, and PTH. The relationship between secondary hyperparathyroidism and CVD in patients with earlier CKD stages has not been fully studied. We sought to evaluate the independent relationship, if any, between PTH level and prevalent CVD in participants in a nationwide CKD screening program.

METHODS

Kidney Early Evaluation Program

The Kidney Early Evaluation Program (KEEP) is a free community-based health screening program that targets populations 18 years and older with a history of diabetes or hypertension or a first-order relative with diabetes, hypertension, or kidney disease. KEEP was launched by the National Kidney Foundation in August 2000 after a pilot program conducted early in 1997 screened about 900 participants. The KEEP database has been fully described previously.[25] Beginning November 1, 2005, PTH tests are performed for participants with eGFR less than 60 mL/min/1.73 m^2. Our study population includes only eligible KEEP participants from November 1, 2005, through December 31, 2007, with eGFR less than 60 mL/min/1.73 m^2.

For these participants, additional reflex calcium and phosphorus testing was performed. Calcium and phosphorus levels were determined using the Architect c8000 (Abbott Laboratories, Abbott Park, IL) with Arsenazo-III dye for calcium and ammonium molybdate for phosphorus. Blood for intact PTH testing was collected in EDTA tubes. The intact PTH assay was performed using Immulite 2000 (Siemens Medical Solutions Diagnostics, Los Angeles, CA), a 2-site chemiluminescent enzyme-labeled immunometric assay. All laboratory tests were conducted at Consolidated Laboratory Services, Van Nuys, CA.

Between November 1, 2005, and December 31, 2007, PTH data were available for 4,772 eligible KEEP participants with eGFR less than 60 mL/min/1.73 m^2. Of these, 29 with eGFR less than 15 mL/min/1.73 m^2 were excluded, and an additional 271 with missing CVD status were excluded. The study cohort for this analysis thus included 4,472 eligible KEEP participants.

Definitions

eGFR was calculated using the isotope dilution mass spectometry–traceable 4-variable Modification of Diet in Renal Disease (MDRD) Study equation,[26] and serum creatinine was calibrated to the Cleveland Clinic Research Laboratory.[27] Albumin-creatinine ratios were calculated from urine samples and recorded as less than 30, 30 to 300, or greater than 300 mg/g. The study targeted only patients with CKD stages 3 to 4, defined as stage 3, eGFR of 30 to 59 mL/min/1.73 m^2, and stage 4, eGFR of 15 to 29 mL/min/1.73 m^2.

Diabetes mellitus was defined as history of diabetes (self-report or retinopathy) or use of medications for diabetes. Hypertension was defined as history of hypertension (self-report) or use of medications for hypertension. Increased blood pressure was defined as systolic blood pressure of 130 mm Hg or greater or diastolic blood pressure of 80 mm Hg or greater. Self-reported CVD included heart attack, stroke, abnormal heart rhythm, heart angioplasty, heart bypass, or heart failure. Participants were asked, "Have you been told by a doctor or health care professional of having any of the following (mark all that apply)? Heart attack, heart bypass surgery, heart angioplasty, stroke, heart failure (fluid in the lungs), abnormal heart rhythm." Obesity was defined as body mass index of 30 kg/m^2 or greater.

Statistical Analysis

Participant characteristics by CVD status were compared for demographic differences; χ^2 test was used to assess the statistical significance of these differences. Multivariate logistic regression was used to estimate the odds ratio (OR) of CVD. Age, hemoglobin level, eGFR, plasma PTH level, serum phosphorus level, and serum calcium level were studied as continuous variables. The Cochran-Armitage trend test was used to study the CVD prevalence trend stratified by plasma PTH levels. Because of gaps in the available data, the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) guideline for target range of intact PTH plasma levels for patients with stages 3 and 4 CKD is opinion based. The recommended target ranges are 35 to 70 pg/mL at stage 3 and 70 to 110 pg/mL at stage 4. Therefore, we also studied PTH levels as tertiles with values less than 35, 35 to 70, and greater than 70 pg/mL. Other controlled variables were sex, race, obesity, smoking status, education, self-reported diabetes, self-reported hypertension, increased blood pressure, and albumin-creatinine ratio.

RESULTS

We compared demographic and health variables (Tables 1 and 2, respectively) between groups with missing CVD status (n = 271) and known CVD status (n = 4,472). There were no statistical differences (all $P \geq 0.10$), except for the increased blood pressure variable ($P = 0.003$). Analysis for events was performed for only par-

Table 1. Demographic Characteristics of the Population

Characteristic	All (N = 4,472)	Parathyroid Hormone (pg/mL) <35 (n = 544)	35-70 (n = 1,689)	<70 (n = 2,239)	*P**
Age (y)	68.3 ± 11.8	66.3 ± 12.0	67.5 ± 11.6	69.4 ± 11.8	<0.001
Women (%)	68.3	70.4	69.3	67.0	0.2
Race (%)					<0.001
White	69.1	76.6	73.2	64.2	
African American	19.8	14.0	14.9	24.9	
Other	11.1	9.4	11.8	10.9	
≥High school education (%)	81.3	84.4	83.6	78.7	<0.001
Current smoker (%)	5.9	6.0	6.1	5.8	0.9
Health insurance coverage (%)	89.9	88.9	89.8	90.1	0.7
Family history† (%)	81.6	81.1	82.8	80.8	0.3

Note: Values expressed as mean ± SD or percent. Parathyroid hormone levels expressed in pg/mL and ng/L are equivalent.
**P* values refer to parathyroid hormone levels.
†Family history of hypertension, diabetes mellitus, or kidney disease.

ticipants with known CVD status, and the blood pressure difference disappeared because the number (n = 271) of participants with missing CVD status was too small.

For the 4,472 eligible participants, mean PTH level was 83.9 ± 57.6 pg/mL, and median value was 71 pg/mL. The 75% and 25% quantiles were 104 and 47 pg/mL, respectively.

Table 2. Health Screening Results

Variable	All	Parathyroid Hormone (pg/mL) <35	35-70	<70	*P**
Body mass index (kg/m^2)	30.3 ± 6.6	29.9 ± 6.3	30.0 ± 6.5	30.6 ± 6.7	0.002
Self-reported diabetes (%)	45.6	51.0	45.1	44.7	0.03
Self-reported hypertension (%)	82.8	80.7	80.2	85.2	<0.001
Increased blood pressure† (%)	71.8	69.4	71.3	72.7	0.3
Systolic blood pressure (mm Hg)	136.8 ± 20.4	135.1 ± 19.7	136.4 ± 19.9	137.5 ± 20.9	0.007
Diastolic blood pressure (mm Hg)	76.4 ± 12.0	75.9 ± 11.0	76.2 ± 11.4	76.8 ± 12.6	0.08
Albumin-creatinine ratio (mg/g)‡					<0.001
<30 (%)	76.7	84.8	82.2	70.7	
30-300 (%)	18.8	12.6	15.0	23.2	
>300 (%)	4.4	2.6	2.8	6.1	
eGFR (mL/min/1.73 m^2)					<0.001
15-30 (%)	5.3	2.6	2.4	8.2	
31-59 (%)	94.7	97.4	97.6	91.8	
eGFR (mL/min/1.73 m^2)	48.2 ± 9.3	50.1 ± 7.9	50.1 ± 8.0	46.3 ± 10.1	<0.001
Anemia§ (%)	22.1	19.9	17.6	26.0	<0.001
Hyperphosphatemia‖ (%)	6.9	9.9	6.9	6.2	0.009
Phosphorus (mg/dL)	3.8 ± 0.7	3.9 ± 0.6	3.8 ± 0.6	3.7 ± 0.7	<0.001
Hypocalcemia¶ (%)	0.5	0.2	0.2	0.9	0.02
Calcium (mg/dL)	9.6 ± 0.5	9.8 ± 0.5	9.6 ± 0.5	9.5 ± 0.5	<0.001

Note: Values expressed as mean ± SD or percent. Conversion factors for units: eGFR in mL/min/1.73 m^2 to mL/s/1.73 m^2, ×0.01667; hemoglobin in g/dL to g/L, ×10; phosphorus in mg/dL to mmol/L, ×0.3229; calcium in mg/dL to mmol/L, ×0.2495. Parathyroid hormone levels expressed in pg/mL and ng/L are equivalent.
Abbreviation: eGFR, estimated glomerular filtration rate.
**P* values refer to parathyroid hormone levels.
†Systolic blood pressure of 130 mm Hg or greater or diastolic blood pressure of 80 mm Hg or greater.
‡Microalbuminuria, 30 to 300 mg/g; macroalbuminuria, greater than 300 mg/g.
§Hemoglobin level less than 13 g/dL in men and less than 12 g/dL in women.
‖Phosphorus level greater than 4.6 mg/dL.
¶Calcium level less than 8.4 mg/dL.

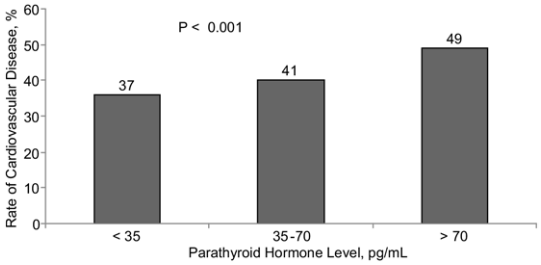

Figure 1. Cardiovascular disease prevalence stratified by parathyroid hormone (PTH) level. $P < 0.001$ for Cochran-Armitage trend test. PTH levels expressed in pg/mL and ng/L are equivalent.

For the total study population, mean age was 68.3 ± 11.8 years; 68% were women, 69% were white, and 6% were current smokers. Grouping by PTH tertiles (Table 1) showed significantly unequal participant distribution for age, race, and educational status. Equal participant distributions for women, smoking status, insurance coverage, and family history of diseases were observed for all tertiles.

For 4,233 participants, eGFR was 30 to 60 mL/min/1.73 m^2, and for 239, eGFR was 15 to 30 mL/min/1.73 m^2. Secondary hyperparathyroidism prevalence was 3,928 (88%), with PTH level greater than 70 pg/mL for 2,239 (50.1%). Of the total population, 45% were obese, 46% had diabetes, 83% had hypertension, 22% were anemic, 18.8% had microalbuminuria, 4.4% had macroalbuminuria, 6.9% had hyperphosphatemia, and 0.5% had hypocalcemia. Grouping by PTH tertiles (Table 2) showed significantly unequal participant distribution for all variables except increased blood pressure.

A total of 1,972 participants self-reported a history of CVD. Non–mutually exclusive categories were 721 self-reported heart attacks, 487 strokes, 1,075 abnormal heart rhythms, 470 angioplasties, 482 heart bypass surgeries, and 357

Table 3. Unadjusted Odds Ratios for Prevalent Cardiovascular Disease

Variable	Odds Ratio (95% confidence interval)	*P*
Age*	1.03 (1.03-1.04)	<0.001
Men	1.45 (1.28-1.65)	<0.001
Race		
White	1.00 (reference)	
African American	0.83 (0.72-0.97)	0.02
Other	0.77 (0.63-0.93)	0.007
Current smoker	1.03 (0.79-1.33)	0.8
≥High school education	0.92 (0.79-1.07)	0.3
Body mass index ≥ 30 kg/m^2	0.93 (0.83-1.05)	0.2
Self-reported diabetes	1.79 (1.58-2.01)	<0.001
Self-reported hypertension	1.87 (1.58-2.20)	<0.001
Increased blood pressure†	0.86 (0.75-0.98)	0.02
Albumin-creatine ratio (mg/g)		
<30	1.00 (reference)	
30-300	1.35 (1.16-1.57)	<0.001
>300	1.66 (1.24-2.22)	<0.001
eGFR‡	0.97 (0.96-0.98)	<0.001
Hemoglobin*	0.93 (0.89-0.97)	<0.001
Phosphorus*	0.99 (0.91-1.08)	0.8
Calcium*	0.85 (0.75-0.95)	0.006
PTH (pg/mL)		
<35	1.00 (reference)	
35-70	1.16 (0.95-1.42)	0.1
>70	1.61 (1.33-1.95)	<0.001
PTH value‡	1.02 (1.01-1.02)	<0.001

Note: PTH levels expressed in pg/mL and ng/L are equivalent.
Abbreviations: eGFR, estimated glomerular filtration rate; PTH, parathyroid hormone.
*Continuous variables.
†Systolic blood pressure of 130 mm Hg or greater or diastolic blood pressure of 80 mm Hg or greater.
‡Per 5-unit increase.

heart failures. Unadjusted prevalent rates of CVD by PTH level are shown in Fig 1, and unadjusted ORs for prevalent CVD are listed in Table 3. The conventional CVD risk factors of age, male sex, African American race, diabetes, and hypertension were significantly associated with CVD prevalence. We noted a trend toward increased CVD prevalence in smokers, but the OR was not statistically significant. Considering CKD components, albumin-creatinine ratio of 30 mg/g or greater was found to be a marker of CVD. CVD prevalence decreased significantly with increased eGFR and increased hemoglobin level; CVD prevalence increased significantly with increased PTH level when tested as a continuous variable (OR, 1.02; 95% confidence interval [CI], 1.01 to 1.02; $P < 0.001$) and for participants with PTH levels greater than 70 pg/mL (OR, 1.61; 95% CI, 1.33 to 1.95; $P < 0.001$), with a nonsignificant relationship of CVD prevalence with serum phosphorus level.

On multiple logistic regression analysis (Table 4), the conventional CVD risk factors of age, male sex, African American race, diabetes, and hypertension were significantly associated with CVD prevalence, and CVD was significantly more prevalent in smokers. Considering CKD components, CVD prevalence significantly increased with decreased eGFR; CVD was common in participants with albumin-creatinine ratios of 30 mg/g or greater and low hemoglobin levels. When plasma PTH level was tested as a continuous variable, increases were significantly associated with increases in CVD prevalence (OR, 1.01; 95% CI, 1.01 to 1.02; $P < 0.001$). When tested as tertiles (Table 5), plasma PTH level greater than 70 pg/mL was significantly associated with CVD prevalence (OR, 1.51; 95% CI, 1.21 to 1.88; $P < 0.001$), with a nonsignificant relationship of CVD prevalence with serum calcium and phosphorus levels.

DISCUSSION

We found in a well-characterized population screened for CKD that secondary hyperparathyroidism with plasma PTH levels greater than 70 pg/mL was common and significantly associated with prevalent CVD. This association was independent of eGFR and calcium and phosphorus levels. It is consistent with the biological charac-

Table 4. Odds Ratios for Cardiovascular Disease From Multivariate Logistic Regression, Parathyroid Hormone as a Continuous Variable

Variable	Odds Ratio (95% confidence interval)	*P*
Age*	1.03 (1.02-1.04)	<0.001
Men	1.51 (1.30-1.77)	<0.001
Race		
White	1.00 (reference)	
African American	0.84 (0.70-1.01)	0.06
Other	0.77 (0.61-0.96)	0.02
Current smoker	1.41 (1.06-1.87)	0.02
≥High school education	1.11 (0.94-1.32)	0.2
Body mass index ≥ 30 kg/m^2	0.98 (0.85-1.13)	0.8
Self-reported diabetes	1.72 (1.50-1.98)	<0.001
Self-reported hypertension	1.43 (1.18-1.73)	<0.001
Increased blood pressure†	0.80 (0.69-0.93)	0.003
Albumin-creatinine ratio (mg/g)		
<30	1.00 (reference)	
30-300	1.13 (0.95-1.34)	0.2
>300	1.21 (0.87-1.70)	0.3
eGFR‡	0.94 (0.90-0.98)	0.003
Hemoglobin*	0.99 (0.94-1.05)	0.8
Phosphorus*	1.09 (0.99-1.21)	0.08
Calcium*	0.99 (0.86-1.14)	0.9
PTH value‡	1.01 (1.01-1.02)	<0.001

Abbreviations: eGFR, estimated glomerular filtration rate; PTH, parathyroid hormone.
*Continuous variables.
†Systolic blood pressure of 130 mm Hg or greater or diastolic blood pressure of 80 mm H or greater.
‡Per 5-unit increase.

Table 5. Odds Ratios for Cardiovascular Disease From Multivariate Logistic Regression, Parathyroid Hormone as Tertiles

Variable	Odds Ratio (95% confidence interval)	*P*
Age*	1.03 (1.02-1.04)	<0.001
Men	1.51 (1.29-1.76)	<0.001
Race		
White	1.00 (reference)	
African American	0.85 (0.71-1.02)	0.08
Other	0.76 (0.61-0.95)	0.02
Current smoker	1.40 (1.05-1.87)	0.02
≥High school education	1.12 (0.94-1.33)	0.2
Body mass index ≥ 30 kg/m^2	0.98 (0.85-1.13)	0.8
Self-reported diabetes	1.73 (1.51-1.99)	<0.001
Self-reported hypertension	1.43 (1.18-1.73)	<0.001
Increased blood pressure†	0.79 (0.68-0.92)	0.002
Albumin-creatinine ratio (mg/g)		
<30	1.00 (reference)	
30-300	1.13 (0.95-1.34)	0.2
>300	1.24 (0.88-1.73)	0.2
eGFR‡	0.93 (0.89-0.97)	<0.001
Hemoglobin*	0.99 (0.94-1.04)	0.8
Phosphorus*	1.10 (0.99-1.21)	0.07
Calcium*	0.99 (0.86-1.14)	0.9
PTH (pg/mL)		
<35	1.00 (reference)	
35-70	1.22 (0.97-1.52)	0.09
>70	1.51 (1.21-1.88)	<0.001

Note: Parathyroid hormone levels expressed in pg/mL and ng/L are equivalent.
Abbreviations: eGFR, estimated glomerular filtration rate; PTH, parathyroid hormone.
*Continuous variables.
†Systolic blood pressure of 130 mm Hg or greater or diastolic blood pressure of 80 mm Hg or greater.
‡Per 5-unit increase.

teristics of CKD mineral and bone disorder, in which PTH is a compensatory hormone working to maintain calcium and phosphorus homeostasis in the setting of reduced vitamin D.

The relationship of CKD and CVD has been described in numerous previous studies. Go et al[4] observed an independent graded association between reduced eGFR and CVD. McCullough et al[28] reported on individual components of CKD, namely anemia and microalbuminuria, as CVD risk states in addition to reduced eGFR. The KDOQI guidelines recommend screening for CKD mineral and bone disorders, including PTH testing, for patients at eGFR less than 60 mL/min/1.73 m^2. The KDOQI recommendations define desirable serum PTH levels at various CKD stages. Our findings provide further support for these guidelines because increased PTH level appears to signal greater risk of prevalent CVD.

Results from our study and others[4,28] suggest that screening for CVD could yield high returns in patients with CKD risk markers, including PTH levels, but who do not report a CVD history. Hyperparathyroidism is one measure of the systemic CKD mineral and bone disorder that is quantifiable by using laboratory testing. High PTH levels have been implicated in patients with myocardial hypertrophy, myocardial fibrosis, myocardial calcium deposition, atherosclerosis, calcification of atherosclerotic lesions, vascular stiffness, and hypertension,[9] all of which may directly contribute to morbidity and mortality from cardiovascular causes secondary to arrhythmias, ischemia, and decreased left ventricular function.

This study has several limitations. Because the mean age of the population was 68 years, these data may not generalize to relatively younger populations. Limitations common to population

screening studies also apply here. Participants were volunteers and likely motivated by their recognized risk of CKD. However, because KEEP screening recruitment materials do not include the terms "heart" or "cardiovascular disease," participants likely enrolled based on concern about CKD, and CVD likely represents a measured variable. Self-reported CVD has inherent variance related to both overreporting and underreporting. Because of the cross-sectional nature of this study, causal relationships between plasma PTH levels and CVD cannot be defined. Because PTH level potentially is modifiable, if a causal relationship could be proved, testing would provide an opportunity to manage PTH levels.

Lipid values were not measured and could be a source of uncontrolled confounding. We did not have electrocardiographic, echocardiographic, or clinical record confirmation of myocardial infarction, stroke, or abnormal heart rhythm. We did not have information regarding the percentage of patients treated for metabolic complications of CKD. Thus, patients with greater plasma PTH levels could have been misclassified to a lower PTH tertile, thereby diluting CVD events in the higher tertile. PTH level increase is in response to decreases in the renal production of 1,25 dihydroxyvitamin D, and hypovitaminosis D itself has been implicated in CVD.[29-32] Vitamin D levels were not measured and could be a source of uncontrolled confounding. This was only partially taken into consideration by related markers (serum calcium and phosphate levels).

The current KDOQI guidelines to maintain intact PTH levels within a defined range of optimal values for each stage of CKD and adjust intact PTH-reducing treatments accordingly were derived from Allegro (Nichols Institute, San Juan Capistrano, CA) intact PTH immunoradiometric assay. In this study, the intact PTH assay was performed using Immulite 2000 (Siemens Medical Solutions Diagnostics, Deerfield, IL), a 2-site chemiluminescent enzyme-labeled immunometric assay. Studies have reported marked variability in circulating PTH values caused by the nature of the assay and/or blood specimen type.[33,34] Because of high intermethod variability in PTH measurement, the association of intact PTH level with CVD may not be comparable when using different methods.

In conclusion, plasma PTH levels greater than 70 pg/mL are significantly associated with prevalent CVD events in patients with CKD stages 3 and 4. Importantly, the association was independent of eGFR and serum phosphorus and calcium levels. These findings provide further support for intact PTH testing, along with testing for other indicators of CKD mineral and bone disorders, at earlier CKD stages.

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