Changes in Cardiovascular Calcification After Parathyroidectomy in Patients With ESRD

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• ***Background:*** **The effect of parathyroidectomy on vascular calcification in patients with end-stage renal disease has been a subject of interest for many years, although studies in this area have not been definitive. The purpose of this investigation is to determine changes in vascular calcification after subtotal parathyroidectomy by using fast-gated helical computed axial tomographic imaging to measure coronary and carotid artery calcification.** ***Methods:*** **Computed tomographic imaging was performed at baseline and in follow-up on 10 patients who had undergone subtotal parathyroidectomy and 10 reference patients who had not undergone parathyroidectomy.** ***Results:*** **Patients who underwent subtotal parathyroidectomy had a mean change in coronary calcification of −92.3 ± 469/y, and reference patients had a mean change of +479 ± 630/y ($P = 0.03$). The 2 parathyroidectomy patients with the highest baseline scores had significant declines in both coronary and carotid calcification.** ***Conclusion:*** **In this study, subtotal parathyroidectomy is associated with a significant decrease in vascular calcification in 2 of 10 dialysis patients with high coronary artery calcium scores and stabilization in 7 of 10 patients with low baseline scores.** ***Am J Kidney Dis*** **46:464-469.**

INDEX WORDS: Vascular calcification; coronary; carotid; end-stage renal disease (ESRD); hemodialysis (HD); peritoneal dialysis (PD); cardiovascular.

THE EFFECT OF parathyroidectomy on vascular calcification in patients with end-stage renal disease has been a subject of interest for many years,[1-3] although studies in this area have not been definitive. This issue is of increasing importance with the identification of cardiovascular calcification as a risk factor for cardiac death.[4] Hemodialysis patients have a very high prevalence of vascular calcification; 83% of patients had coronary calcification in a cross-sectional study of 205 hemodialysis patients.[5] In addition, dialysis patients disproportionately experience cardiovascular death, with approximately 42% of dialysis patient deaths in the US Renal Data System recorded as cardiovascular in origin.[6] Therapeutic interventions that stabilize or potentially reverse calcification may be of great value to patients with end-stage renal disease with vascular disease.

Prior studies investigating the relationship between vascular calcification and parathyroidectomy were limited by the use of radiological techniques that could only grossly quantify calcification.[1,3] Recent advances in computed tomographic (CT) scanning of coronary arteries now allow us to more accurately quantitate vascular calcium content.[4] In the present study, we report on a group of patients who underwent subtotal parathyroidectomy and gated CT scanning of the coronary and carotid arteries before and after subtotal parathyroidectomy.

METHODS

This study was approved by the Wake Forest University School of Medicine (Winston Salem, NC) Institutional Review Board.

Population

Individuals undergoing peritoneal dialysis or hemodialysis at dialysis centers in the southeastern United States operated by Wake Forest University School of Medicine who were to undergo subtotal parathyroidectomy for elevated intact parathyroid hormone (iPTH) levels refractory to medical therapy were invited to participate in the study. A

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Table 1. Baseline Characteristics of Subtotal Parathyroidectomy and Reference Patients

Characteristic	Parathyroidectomy (n = 10)	Reference (n = 10)	*P*
Age (y)	44.8 ± 11.4	54.4 ± 16.8	0.15
Race (% white)	2 (20.0)	6 (60.0)	0.17
Sex (% male)	5 (50.0)	4 (40.0)	0.99
Vintage (y on hemodialysis)	6.7 ± 5.2	4.5 ± 3.8	0.28
Modality (% hemodialysis)	9 (90.0)	7 (70.0)	0.58
Baseline iPTH (pg/mL)	926.2 ± 628.5	151.2 ± 80.8	0.0036
Baseline adjusted serum calcium (mg/dL)	9.0 ± 1.2	10.1 ± 1.5	0.064
Baseline serum phosphorus (mg/dL)	6.7 ± 1.6	4.8 ± 1.4	0.024
Baseline serum calcium × phosphorus product (mg^2/dL^2)	56.7 ± 17.0	49.2 ± 17.0	0.33

NOTE. To convert iPTH in pg/mL to ng/L, multiply by 1; serum calcium in mg/dL to mmol/L, multiply by 0.2495; serum phosphorus in mg/dL to mmol/L, multiply by 0.3229; calcium phosphorus product in mg^2/dL^2 to $mmol^2/L^2$, multiply by 0.0808.

reference group of dialysis patients who had not undergone parathyroidectomy also was included.

Coronary artery calcification (CAC) was measured by using fast-gated helical CT as previously described.[7] Scans were performed on 2 single-slice subsecond helical CT scanners equipped for retrospective cardiac gating and capable of 500-millisecond temporal resolution (HiSpeed LX with the SmartScore Cardiac scan package; General Electric Medical Systems, Milwaukee, WI). Scanning of the entire heart and carotid arteries was performed during suspended respiration at end-inspiration. The scan was obtained at 50% of the RR interval. Scanning of cardiac vessels was performed twice, and results were averaged. CAC score was determined by using a modified Agatston method with the traditional 130-Henry U threshold and a minimum lesion definition of 0.52 mm^2. This method has an extremely high correlation with electron-beam CT–derived CAC scores (r = 0.98) based on a previous investigation we performed.[8]

Carotid scans were performed measuring calcified plaque burden in the common carotid, internal carotid, external carotid, and bulb. These measurements were averaged for the left and right sides.[9]

Baseline fast-gated helical CT scans were performed at the time of subtotal parathyroidectomy in 10 individuals. Follow-up scans were performed during a 2-year period. Timing of follow-up scans was determined by the desire for increased length of follow-up. Scans were performed in a similar manner for the reference group. Mean carotid score was the average of the right and left carotid scores.

Medical records and dialysis records for each patient were reviewed to determine demographics, phosphate-binder use, and monthly laboratory values between scans. Calcium binder dosage was converted to the amount of elemental calcium for each preparation. Vitamin D dosage was converted to the equivalent amount of calcitriol, assuming a 3:1 conversion for doxercalciferol or paricalcitol to calcitriol. Chemistry values and medication dosages were time-averaged over the duration between the 2 scans.

PTH was measured as iPTH by using a solid-phase 2-site chemiluminescent enzyme-labeled immunometric assay on the Immulite 2000 (Diagnostic Products Corp, Los Angeles, CA). The reference range for this assay is 11 to 67 pg/mL (ng/L).

Statistical Analysis

Descriptive statistics, including means and SDs for continuous data and frequencies and proportions for categorical measures, were generated for both study groups. Independent *t*-tests were used to test for differences in continuous data, and for dichotomous data, chi-squared tests were used to assess differences between groups. In comparing coronary calcification, several methods were used. First, the difference between the modified Agatston score at baseline and follow-up was determined for each patient and adjusted for the time between scans. *t*-Test comparison of adjusted Agatston scores then was performed. Square-root transformation also was performed and compared between the 2 groups. A volumetric score also was obtained and compared between the 2 groups, as was square-root transformation of the volumetric score. For carotid artery scores, a similar method was used with comparison of baseline and follow-up scans adjusted for time, using both scores and square-root transformation of the scores.

Variability between the modified Agatston scores was determined by obtaining the difference between the 2 CAC scores obtained and dividing by mean CAC score.

RESULTS

Table 1 lists baseline demographic data for the 2 groups. Parathyroidectomy patients were more likely to have elevated iPTH levels and greater serum phosphorus values.

Table 2 lists time-averaged laboratory values, time-averaged phosphate-binder dosage (in grams of elemental calcium per day), and time-averaged calcitriol-equivalent intake (in micrograms per week). Patients who underwent subtotal parathyroidectomy had lower serum calcium and higher serum phosphorus values, whereas calcitriol-equivalent dosages and oral calcium dosages were much greater. Of interest, iPTH levels were similar in follow-up between the 2 groups.