Natural history of vascular calcification in dialysis and transplant patients

Sharon M. Moe1,3, Kalisha D. O’Neill1, Martina Resterova1, Naomi Fineberg1, Scott Persohn2 and Cristopher A. Meyer2

Departments of 1Medicine and 2Radiology, Indiana University School of Medicine and 3Roudebush Veterans Affairs Medical Center, Indianapolis, IN, USA

Abstract

Background. The purpose of the present study was to determine the natural history of coronary artery and aorta calcification by spiral computed tomography (CT) in patients who undergo a renal transplant and patients on haemodialysis.

Methods. Two cohorts were evaluated for the natural history of vascular calcification: (i) 23 patients who underwent a baseline CT scan at the time of renal transplant and a repeat evaluation 15–20 months later; and (ii) 33 chronic kidney disease, stage 5 haemodialysis subjects who underwent a baseline CT scan, all followed for a minimum of 15 months, and 17 of whom underwent a second CT scan.

Results. In the patients undergoing a renal transplant, there was no net change in CAC with time, suggesting stabilization of calcification. In the haemodialysis patients, the median CAC increased by 1.27±1.88 score/days, \( P = 0.013 \). There was a trend towards increasing AoC score in both groups. All patients without calcification at baseline remained calcification free at follow-up. In the 15 months following baseline, the six dialysis patients who died had a significantly greater CAC score at baseline compared with the 24 patients who remained alive. Similarly, those patients who were hospitalized had a greater baseline CAC than patients who were not hospitalized.

Conclusion. In this preliminary study, renal transplantation appears to slow down or arrest CAC, whereas CAC progresses in haemodialysis patients. In haemodialysis patients, CAC was greater in patients who died or were hospitalized compared with those who remained alive or were not hospitalized.

Keywords: coronary artery disease; dialysis; renal transplant; spiral CT; vascular calcification

Introduction

Atherosclerotic disease remains a major cause of morbidity and mortality in the general population. The assessment of coronary arteries by new imaging techniques such as electron beam computed tomography (EBCT) scan and intravascular ultrasound has heightened the awareness that most atherosclerotic plaques observed in the ageing population are calcified. Furthermore, in non-dialysis patients, the magnitude of calcification by EBCT correlates with the severity of obstructive coronary artery disease by angiography and with clinical cardiac events [1]. Cardiovascular disease and stroke are the leading cause of death in patients with end-stage renal disease who require dialysis [chronic kidney disease, stage 5 (CKD-5)], at a risk that is 10- 20-fold that of the age- and sex-matched general population [2,3]. A study evaluating coronary calcification by EBCT in patients with CKD-5 has demonstrated 2- to 5-fold more coronary artery calcification than age- and sex-matched individuals with angiographically proven coronary artery disease. Furthermore, in a follow-up of these 57 haemodialysis patients, every patient had an increase in their calcification score when followed-up just 1–2 years later [4]. Goodman et al. demonstrated that this process also affects young adults on dialysis, with a sharp increase in the magnitude of coronary artery calcification by EBCT after age 20 [5]. These results imply that the presence of vascular calcification may have prognostic implications for dialysis patients. Indeed, the greater the degree of vascular peripheral calcification by ultrasound [6] and plain radiographs [7], the greater the risk of mortality. However, such prospective outcome data are lacking for coronary artery vascular
calcification scores by EBCT or spiral CT in CKD, although coronary artery calcification scores by EBCT have been shown to correlate with a history of cardiovascular disease [8].

The aetiology of vascular calcification in CKD-5 patients is most probably multifactorial. Older age and longer time on dialysis (‘vintage’) are prominent risk factors in a number of studies assessing vascular calcification by various techniques [4,5,7,9,10]. We recently have described the use of quad-slice spiral (helical) CT scan with gating in CKD-5 patients, demonstrating the usefulness of this technique and confirming that increased age and duration of dialysis are risk factors for vascular calcification in the coronary arteries [10]. In addition, some studies have demonstrated that dyslipidemia, systolic hypertension and disorders of mineral metabolism, including elevated phosphorus and/or calcium phosphorus product, and calcium load in the form of phosphate binders, are significant risk factors for vascular calcification [5,7,9].

Renal transplantation improves disorders of mineral metabolism, and removes many uraemic toxins; therefore, renal transplantation may improve vascular calcification. However, transplantation is also pro-atherogenic, with induction of hyperglycaemia/glucose intolerance, hyperlipidaemia and hypertension by the various immunosuppressive agents [11]. Cardiovascular mortality remains greater in transplant patients than in the general population, although it is less than in patients undergoing dialysis [2]. Thus, renal transplantation may trade one set of vascular calcification risk factors for another. To date, there are no published studies describing the natural history of coronary artery calcification in patients with CKD-5 who undergo a renal transplant. The purpose of the present study was to determine the natural history of vascular calcification in patients with CKD-5 who remain on haemodialysis and in those who receive a functioning renal transplant.

Subjects and methods

Two patient groups were examined: group 1, patients with CKD-5 undergoing a renal transplant (hereafter referred to as ‘transplant’); and group 2, patients with CKD-5 undergoing chronic haemodialysis (hereafter referred to as ‘dialysis’). The baseline characteristics and coronary artery and aorta calcification scores of these two patient populations have been described in detail previously [10], with important differences in these two populations precluding a direct comparison of transplant and dialysis. Thus each group is presented separately. The study was approved by the Institutional Review Board and all patients gave written informed consent.

Transplant patients

Patients were recruited at the time of admission to hospital for transplantation, with a large and diverse referral base from all over the state of Indiana. The patients underwent the baseline spiral CT scan within 3 days after the transplant. Medications, other medical illnesses and demographic factors were obtained from history and/or review of the patients’ chart. Baseline laboratory values were analysed from predialysis chemistry assays if the patient underwent a dialysis immediately prior to the transplant, or from sera collected at the time of transplant. All patients were asked to undergo a second spiral CT scan 15–20 months after the renal transplant. Additional serum was collected at the time that the patient underwent the second spiral CT. Medications and rejection episodes/therapy were reviewed from the medical record and patient history. Creatinine clearance was calculated by the MDRD formula using data obtained within 1 month of the follow-up spiral CT.

Dialysis patients

Patients undergoing chronic haemodialysis at Indiana University were asked to participate in the study and underwent a spiral CT scan after obtaining informed consent. The only inclusion criteria were age greater than 18 years, able to give informed consent, not in atrial fibrillation, and no metallic objects in the chest (clips or valves) due to the potential for causing artefacts with the CT scan. Baseline laboratory values were averaged from the previous 12 months for chemistries, parathyroid hormone (PTH), alkaline phosphatase and cholesterol. A serum sample was obtained at the time of consent for other laboratory tests. A second sample was analysed 3–4 months later for an additional C-reactive protein (CRP) measurement because of the possibility of intermittent increases in the level of this protein. The two values for CRP were averaged to obtain the ‘baseline’ value.

Serum assays

Serum was analysed for calcium, phosphorus and total alkaline phosphatase by colorimetric methods using a Roche Autoanalyzer (Boehringer Mannheim, Indianapolis, IN), intact PTH by immunoradiometric assay (Nichols Institute, San Juan Capistrano, CA), bone-specific alkaline phosphatase by enzyme-linked immunosorbent assay (ELISA; Metra Biosystems, Mountain View, CA), homocysteine by ELISA (Bio-rad) and CRP by ELISA (Alpha Diagnostics, San Antonio, TX).

Spiral CT scan

CT scans were performed with the quad-slice technique on the model MX 8000 scanner (Philips Medical Systems, Cleveland, OH) as previously described in detail [10]. The data acquisition parameters were: 120 kVp, 400 mAs, nominal slice width 2.5 mm (effective width 3.2 mm), gantry rotation time 0.5 s, table speed 7.5 mm/s [pitch 0.375 (× 4 slices/rotation)]. Data were reconstructed with a 180° linear interpolation algorithm.
providing a temporal resolution of 270 ms, retrospective electrocardiograph (ECG) gating during diastole, 1.3 mm longitudinal increment, 512 × 512 matrix, field of view 25 cm, medium body (C) filter, and no edge enhancement. Data were transferred to a workstation and analysed with HeartBeat-CS software (MX View, Marconi Medical Systems, Cleveland, OH). On the basis of the ECG tracing during the scan, the software program automatically selected a reduced set of diastolic images from each cardiac cycle to accurately reflect diastole (‘retrospective gating’). The proximal coronary arteries were scored, beginning with the first image in which a coronary artery was seen (usually the left anterior descending) and continuing for 6 cm along the long axis of the patient [12]. All pixels with density ≥130 Hounsfield units (HU) were highlighted automatically in colour on the images. The observer placed an electronic region of interest (ROI) around each highlighted coronary artery calcification and assigned one of four locations to each calcified plaque: left main, left anterior descending (LAD), circumflex or right coronary artery. Branches were considered parts of those arteries. The cumulative score of all coronary arteries is the coronary artery calcium score. The descending aorta was evaluated over 6 cm in the z-axis direction. A minimum plaque area of 0.5 mm² was used to reduce errors due to noise. All scans were reviewed by a single reader (C.A.M.) who was blinded to any clinical information about the subject. Calcium scoring was performed using two scoring systems as previously detailed [10], an area-based method simulating the method of Agatston et al. [12], and a volume-based method. As previously reported, these two methods are closely related (r = 0.99, P < 0.001 [10]). Because of this, and for clarity, only volume-based measures are provided in the present report.

For a minority of scans done in the transplant patients at baseline, the gating software was not yet available. To control for this, additional gated and non-gated scores were done in 15 patients and a formula derived to convert non-gated to gated, as previously described [10]. The results for the present study are all gated scans, with 10 baseline gated scans derived from this conversion formula. To validate this, change in calcification in these 10 subjects was also assessed using only non-gated scans, and this did not affect the results. Of importance, of these 10 subjects who were scanned initially without gating, four had no coronary artery calcification, thereby minimizing any impact of this conversion factor.

As previously reported, the intra-reader variability was a mean of 0.9 and 2.9% for coronary artery calcification score by area and volume and 6% for aorta calcification score by area and volume [10]. All but one scan read as no calcification at baseline had results previously reported [10]. Twenty-three underwent a follow-up scan. One patient died (shortly after transplant from a stroke), one transplant failed, and 13 moved away or refused to return to the medical centre for a follow-up scan. The baseline characteristics of the transplant subjects were described previously [10], and there was no difference in age, duration of dialysis, type of dialysis, gender, race and diabetes in those who did and did not undergo a follow-up scan. Similarly, there was no difference in baseline intact PTH, calcium, phosphorus, CRP and homocysteine levels in those who did vs those who did not undergo a follow-up scan. Thus, for the present report, only the patients who underwent two scans are evaluated, and are unlikely to reflect a biased follow-up. The baseline and follow-up coronary artery and aorta calcification scores are shown in Table 1. The individual changes in coronary calcification in patients with calcification present at baseline are shown in Figure 1A. The coronary artery calcification score change/days was not significant (0.181 ± 0.611 score/day).

### Statistical methods

For each group, the difference between calcification score at the second scan and score at the first scan has been divided by the number of days between scans. A negative value implies an improvement (less calcium deposited at the time of the second scan), and a positive value indicates an increase in calcification. The change/days were analysed by one-group t-test comparing the change/days with zero. Spearman correlation was used to correlate changes in score over time and possible predictive factors (baseline score, age, months on dialysis, PTH, alkaline phosphatase, homocysteine and CRP). Comparisons of baseline and interval laboratory and medications in dialysis patients with progressive calcification vs those without were analysed using t-tests for continuous variables, Fisher’s exact test for discrete variables and the Mann–Whitney U-test for non-normally distributed continuous variables. Mann–Whitney U-tests were used to assess the correlation with diabetes mellitus and history of coronary artery disease. To determine the relationship of calcification score to death or hospitalization, a Mann–Whitney U-test was done for continuous variables, and Fisher’s exact test for categorical variables. All values are expressed as mean ± SD, with a P < 0.05 considered significant.

### Results

#### Transplant subjects

Thirty-eight patients undergoing a transplant had a baseline CT scan, with results previously reported [10]. Twenty-three underwent a follow-up scan. One patient died (shortly after transplant from a stroke), one transplant failed, and 13 moved away or refused to return to the medical centre for a follow-up scan. The baseline characteristics of the transplant subjects were described previously [10], and there was no difference in age, duration of dialysis, type of dialysis, gender, race and diabetes in those who did and did not undergo a follow-up scan. Similarly, there was no difference in the baseline intact PTH, calcium, phosphorus, CRP and homocysteine levels in those who did vs those who did not undergo a follow-up scan. Thus, for the present report, only the patients who underwent two scans are evaluated, and are unlikely to reflect a biased follow-up. The baseline and follow-up coronary artery and aorta calcification scores are shown in Table 1. The individual changes in coronary calcification in patients with calcification present at baseline are shown in Figure 1A. The coronary artery calcification score change/days was not significant (0.181 ± 0.611 score/day).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coronary artery calcification</th>
<th>Aorta calcification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline coronary artery calcification score</td>
<td>269 ± 472</td>
<td>146 ± 431</td>
</tr>
<tr>
<td>Final coronary artery calcification score</td>
<td>346 ± 649</td>
<td>179 ± 519</td>
</tr>
<tr>
<td>Delta calcium score</td>
<td>77 ± 246</td>
<td>34 ± 96</td>
</tr>
<tr>
<td>Days between scans</td>
<td>457 ± 60</td>
<td>457 ± 60</td>
</tr>
<tr>
<td>Delta calcium score/day</td>
<td>0.181 ± 0.611*</td>
<td>0.069 ± 0.182*</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SD, median (range). *P = 0.169; **P = 0.85.
followed clinically prospectively for a minimum of 15 days; \( P = 0.169 \). In contrast, there was a trend toward an increase in the aorta calcification score (0.069 ± 0.182 score/day; \( P = 0.085 \)). Based on these data, a larger study (at least 57 subjects) may have demonstrated a significant increase over time in aorta calcification. In all subjects, if no calcification was found in the coronary arteries or aorta at baseline, no calcification was found at follow-up. If only those subjects with calcification at baseline were considered, there was still no net change in aorta calcification score over time, and review of records found no clear explanation for this.

Dialysis subjects

Thirty haemodialysis subjects underwent a baseline CT scan and 17 underwent a follow-up study; six subjects died, three underwent a renal transplant, and six refused or had moved. However, all patients were followed clinically prospectively for a minimum of 15 months, or until death, to identify cardiac events and hospitalizations. For patients remaining on dialysis and undergoing two scans, the coronary artery calcification score increased significantly over time (1.27 ± 1.88 change in score/day, \( P = 0.013 \), Table 2). The individual changes in the coronary artery calcification scores in patients with calcification present at baseline are shown in Figure 1B. There was a non-significant trend toward an increase in aorta calcification with time (\( P = 0.091 \), Table 2). In the dialysis patients, the only baseline factors that were associated with a change in calcification in the coronary arteries were baseline calcification score (\( r = 0.77, P < 0.001 \)) and age (\( r = 0.75, P = 0.001 \)), whereas only age was related to change in aorta calcification score (\( r = 0.72, P = 0.001 \)).

All of the haemodialysis patients with no coronary artery calcification at baseline remained without calcification on follow-up, and a similar finding was seen with aorta calcification. There was no difference in interval (between scan) biochemical data, medications or demographic factors in the patients who developed coronary artery calcification (i.e. to those who had baseline calcification) compared with those who remained calcification free, with the exception that patients with calcification were older (\( P = 0.007 \)) and had a higher haemoglobin (\( P < 0.01 \); Table 3). If only those patients with calcification at baseline were evaluated, the change in coronary artery calcification over time was 1.080 (range 0.023–6.077).

All dialysis patients who underwent baseline scanning were followed for 15 months, regardless of whether or not they underwent a second CT scan. The six dialysis patients who died in the 15 months following baseline scan had a significantly greater coronary artery calcification score at baseline (median 1543, range 313–9941) compared with the 24 patients who remained alive (median 54, range 0–3913; \( P = 0.003 \), Figure 2). However, this was potentially confounded by the presence of diabetes (\( P = 0.049 \)), and a trend towards increasing age (\( P = 0.07 \)) also predicting death. Interval serum levels of calcium, phosphorus, calcium–phosphorus product and months on dialysis were not different between those who died.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coronary artery calcification</th>
<th>Aorta calcification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline coronary artery</td>
<td>482 ± 1089 (0 to 5553)</td>
<td>1023 ± 2680 (0 to 10695)</td>
</tr>
<tr>
<td>Final coronary artery</td>
<td>982 ± 1613 (0 to 9950)</td>
<td>1793 ± 3089 (5.5 to 9.950)</td>
</tr>
<tr>
<td>Delta calcium score/day</td>
<td>1.270 ± 1.875* (0.295 to 6.077)</td>
<td>1.898 ± 4.349* (0 to 16.049)</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SD, median (range).

* \( P = 0.13 \); *P = 0.91 by one-group \( t \)-test.

---

**Fig. 1.** Change in coronary artery calcification over time. The changes in coronary artery calcification in transplant recipients (A) and haemodialysis subjects (B) are plotted for individual subjects who had calcification at baseline. Note the logarithmic scale. In both groups, patients without calcification at baseline continued to have no calcification at follow-up (data not shown).
and those who were alive. Similarly, there was a significant difference in the baseline coronary artery calcification score in patients who were hospitalized for non-access reasons (median 561, range 0–8772) compared with those who were never hospitalized for non-access reasons (median 9, range 0–1256; \( P = 0.04 \)) in the 15 months after the initial scan. There was no demographic or laboratory value that confounded the difference between patients who were hospitalized compared with those who were not hospitalized. There was no difference in the aorta calcification score in patients who were dead vs alive, or who were hospitalized vs not hospitalized.

**Discussion**

Cardiovascular disease remains the leading cause of mortality in patients on dialysis and in those with a functioning renal transplant [2,11]. In the present study, we demonstrated that coronary artery calcification stabilizes in subjects who had received a functioning renal allograft. While these results should be considered preliminary due to our small sample size, this is the first study to our knowledge that has determined the natural history of coronary artery calcification after renal transplant and provides yet another example of the positive aspects of transplantation on the ill effects of uremia. In addition, we confirmed previous studies [4,5] that coronary artery calcification progressed in patients on dialysis. We also demonstrated that greater coronary artery calcification is associated with all-cause mortality and hospitalizations in the dialysis patients. These results are the first to demonstrate such a difference in mortality with coronary artery calcification by CT-based imaging. These latter results were unexpected given the small sample size and clearly should be considered preliminary, but are consistent with recent studies demonstrating that the extent of peripheral calcification of the femoral, aorta and carotid arteries by ultrasound [6] and iliac and femoral arteries by plain radiographs [7] were predictive of all-cause and cardiovascular mortality. Similarly, studies in the general population with an EBCT scan demonstrate that coronary artery calcification is predictive of cardiac events and that calcification is additive of traditional Framingham risk factors in predicting ‘hard’ cardiovascular end-points (reviewed in [1]).

**Table 3.** Comparison of haemodialysis patients with two scans who have coronary artery calcification and those without

<table>
<thead>
<tr>
<th></th>
<th>Without calcification (( n = 5 ))</th>
<th>With calcification (( n = 12 ))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>40 ± 5</td>
<td>55 ± 9*</td>
</tr>
<tr>
<td>Duration of HD</td>
<td>96 ± 116</td>
<td>73 ± 56</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0 yes, 5 no</td>
<td>2 yes, 10 no</td>
</tr>
<tr>
<td>Interval mean intact PTH (pg/ml)</td>
<td>227 ± 185</td>
<td>338 ± 230</td>
</tr>
<tr>
<td>Interval mean calcium (mg/dl)</td>
<td>9.2 ± 0.3</td>
<td>8.8 ± 0.8</td>
</tr>
<tr>
<td>Interval mean phosphorus (mg/dl)</td>
<td>5.1 ± 0.9</td>
<td>5.8 ± 1.1</td>
</tr>
<tr>
<td>Interval mean Ca × P (mg²/dl²)</td>
<td>46 ± 10</td>
<td>50 ± 9</td>
</tr>
<tr>
<td>Interval mean alkaline phosphatase (IU)</td>
<td>119 ± 48</td>
<td>181 ± 124</td>
</tr>
<tr>
<td>Final bone alkaline phosphatase (mg/ml)</td>
<td>18.9 ± 10.2</td>
<td>25.1 ± 22.5</td>
</tr>
<tr>
<td>Interval mean cholesterol (mg/dl)</td>
<td>161 ± 25</td>
<td>160 ± 33</td>
</tr>
<tr>
<td>Interval mean Hb (g/dl)</td>
<td>11.2 ± 0.9</td>
<td>12.6 ± 1.4*</td>
</tr>
<tr>
<td>Interval calcium load from phosphate binders (mg/day)</td>
<td>535 ± 224</td>
<td>636 ± 524</td>
</tr>
<tr>
<td>Interval sevelamer</td>
<td>1 yes, 4 no</td>
<td>7 yes, 5 no</td>
</tr>
<tr>
<td>Interval vitamin D therapy</td>
<td>4 yes, 1 no</td>
<td>11 yes, 1 no</td>
</tr>
<tr>
<td>Interval statin therapy</td>
<td>1 yes, 4 no</td>
<td>4 yes, 8 no</td>
</tr>
<tr>
<td>Final homocysteine (µmol/l)</td>
<td>27.4 ± 8.5</td>
<td>28.2 ± 8.1</td>
</tr>
<tr>
<td>Final CRP (µg/ml)</td>
<td>10.8 ± 9.5</td>
<td>13.7 ± 13.9</td>
</tr>
</tbody>
</table>

Mean ± SD, *\( P < 0.01 \) comparing without vs with calcification.

Fig. 2. Coronary artery calcification score related to morbidity and mortality. Dialysis patients were followed for 15 months after the baseline spiral CT scan. Deaths and hospitalizations (for non-access-related conditions) were assessed. The coronary artery calcification score was greater in patients who died compared with those who were alive (\( P = 0.003 \)), and the calcification score was greater in those patients who were hospitalized vs those not hospitalized (\( P = 0.042 \)). Note the logarithmic scale so that data points = 0 are not plotted.
Together with our findings, these results support the finding that in dialysis patients, increased coronary artery and peripheral artery calcification is associated with a detrimental outcome.

Cardiovascular disease is the leading cause of mortality in renal transplantation, and the duration of dialysis prior to transplantation is a strong predictor of post-transplant cardiovascular events [13]. As previously reported, the baseline coronary artery calcification scores in both groups of patients (haemodialysis and transplant recipients) were dependent on age and duration of dialysis [10]. In the present study, there was an overall stabilization of coronary artery calcification in the renal transplant recipients. It is not known if the magnitude of coronary artery calcification at the time of renal transplantation correlates with cardiovascular risk post-transplant, but if this proves to be the case, assessment of coronary artery calcification may become a non-invasive screening tool for such patients. Improvements in assessment of cardiovascular disease are needed, as many transplant candidates have asymptomatic heart disease [11]. While some individuals had minor decreases in coronary artery calcification scores post-transplant, it is not clear if this represents normal variability in the assessment by this method or a true regression of calcification. Conversely, some patients had mild increases in their scores, and one patient had a large increase in coronary artery calcification (Figure 1). There was no obvious explanation for the progression in this particular patient. These variable results demonstrate the heterogeneity of factors that may be associated with coronary artery calcification.

The traditional Framingham risk factors for cardiovascular disease in dialysis patients do not completely account for the increased cardiovascular mortality in dialysis patients compared with the general population [3], and dialysis-specific risk factors such as lipid oxidation, altered mineral metabolism, advanced glycation end-products and other uraemic toxins may be causative. Indeed, we have demonstrated that pooled uraemic serum, regardless of phosphorus concentration, can induce vascular calcification in vitro [14,15]. Many of these factors may lead to both atherogenic disease with secondary calcification and primary medial calcification. To date, we do not have direct pathological evidence as to whether coronary artery calcification seen by spiral CT and EBCT represents calcified intimal/atherogenic disease, medial calcification or both. However, a recent study did not find a correlation with calcification score of individual arteries by EBCT with the magnitude of obstructive atheromatous disease by angiography [16], implying that the excess calcification in the coronary arteries compared with patients with known coronary artery disease [4] may be medial in location. Supporting an important role for adverse outcomes with medial calcification is a recent study by London et al. demonstrating that both intimal and medial arterial calcification occurs in peripheral arteries in dialysis patients, and the presence of either leads to increased mortality compared with no calcification [7]. Thus, both forms of calcification (intimal/atherogenic plaque and medial) may contribute to cardiovascular mortality, but by different mechanisms. Atherogenic lesions will lead to more obstructive lesions and acute angina or myocardial infarction, whereas medial lesions may lead to reduced perfusion of the myocardium, arrhythmias and sudden death. Clearly, we need pathological correlates to coronary artery and aorta imaging to elucidate these differences further. Nonetheless, there is now clear evidence in peripheral arteries that both forms of calcification in dialysis patients contribute to mortality [7], and our findings suggest a similar association for coronary artery calcification. However, our results may have been biased in that individuals who had known coronary artery disease may have been more interested in participating in the study, although we did not specifically target such individuals. Clearly, our observations need to be repeated in a much larger cohort to conclude definitively that increased coronary artery calcification predicts adverse outcomes in dialysis patients.

In conclusion, coronary artery calcification in CKD-5 patients is significantly greater in patients who die, or are hospitalized compared with those who remain alive or are not hospitalized. In addition, renal transplantation appears to slow down or arrest the process in most patients. In both groups of patients, there was a trend towards an increase in the aorta calcification scores with time. Lastly, there is a subset of patients without calcification who remain calcification free, suggesting the presence of protective factors. These results need to be confirmed in larger studies, as does a direct comparison of different forms of renal replacement therapy with matching of subjects for, at minimum, age and duration of dialysis. Nonetheless, these data do suggest that assessment of the magnitude of coronary artery calcification by spiral CT may be predictive of future morbidity and mortality.

Acknowledgements. Supported by funding from the National Kidney Foundation of Indiana and the National Institutes of Health/NIDDK (S.M.M.). This work was presented at the American Society of Nephrology Annual Scientific Meeting in November, 2002.

Conflict of interest statement. None declared.

References


Received for publication: 29.10.03
Accepted in revised form: 7.4.04