Nephrol Dial Transplant (2007) 22: 3208–3213
doi:10.1093/ndt/gfm377
Advance Access publication 7 July 2007

Orignial Article

NDT
Nephrology Dialysis Transplantation

Detection of coronary and peripheral artery calcification in patients with chronic kidney disease stages 3 and 4, with and without diabetes

Christine J. Porter[1], Aristeidis Stavroulopoulos[1], Simon D. Roe[1], Kate Pointon[2] and Michael J.D. Cassidy[1]

[1]Nottingham Renal and Transplant Unit and [2]Department of Radiology, Nottingham University Hospitals NHS Trust, City Campus, Hucknall Road, Nottingham, Ng5 1PB, United Kingdom

Abstract

Background. The purpose of this study was to describe the prevalence and extent of coronary artery calcification (CAC) in subjects with chronic kidney disease (CKD) stages 3 and 4 comparing those with and without diabetes. We also wished to determine if the presence of peripheral artery calcification (PAC) would assist in identifying patients positive for CAC.

Methods. CAC was detected by multi-slice computed tomography and PAC was detected by plain foot radiography. Study population was 112 patients, 54 with diabetes and 58 without, all asymptomatic for heart disease. Demographic and laboratory data were collected and analysed.

Results. The prevalence of CAC in CKD patients was 76 and 46.5% with and without diabetes, respectively. Patients with diabetes had higher CAC scores with more vessels affected, and in the presence of diabetes men and women had the same risk for CAC. In patients with diabetes, age was the unique explanatory variable for detecting the presence of CAC, while age and smoking history predicted severity. In patients without diabetes, age, male gender, body mass index, estimated glomerular filtration rate and serum phosphate levels predicted the presence of CAC, while parathyroid hormone predicted severity. Prevalence of PAC was 63 and 12% in subjects with and without diabetes. PAC detected by foot radiography was not an adequate alternative-screening marker for identifying patients with CAC..

Conclusions. CAC is common in CKD stages 3 and 4 patients, especially in men and women with diabetes.

Keywords: coronary artery calcification; chronic kidney disease; diabetes; gender; multi slice computed tomography; peripheral artery calcification; prevalence

Correspondence and offprint request to: Christine Porter, Nottingham Renal and Transplant Unit, Nottingham University Hospitals NHS Trust, Hucknall Road, Nottingham, NG5 1PB, United Kingdom. Email: christine.j.porter@nuh.nhs.uk

Introduction

In the general population, the presence and extent of coronary artery calcification (CAC) have been used for the non-invasive diagnosis of coronary artery disease in both symptomatic and asymptomatic patients [1,2]. The presence and extent of CAC also seems to have prognostic value for future cardiac events in both asymptomatic and symptomatic patients [2].

Electron beam computed tomography (EBCT) and more recently multislice computed tomography (MSCT) have been used for the detection of CAC and its quantification (CAC score). MSCT is more widely available than EBCT and CAC scores measured with both techniques have similar significance [3].

Vascular calcification is a common complication of chronic kidney disease (CKD) and may contribute to the increased cardiovascular disease (CVD) risk in CKD patients. CAC is virtually never detected in healthy asymptomatic subjects before the age of 40 years [4], yet, it occurs at an early age in haemodialysis patients, demonstrated both by EBCT [5,6] and at post mortem [7]. In patients new to haemodialysis, the prevalence of CAC has been reported at 64%, indicating that the process of calcification begins in the earlier stages of CKD [8,9]. In patients established on dialysis, CAC prevalence rates up to 92% have been reported, and the extent of CAC is up to 10 times greater than expected for age and sex [5,6,10–13]. Studies to date reporting CAC prevalence in CKD patients not undergoing dialysis, report prevalence rates between 27–94% depending upon the case mix [14–18]. Severity of CAC may have prognostic significance in CKD as it has been linked to all-cause mortality [19]. The most consistent predictors of CAC are age, diabetes and dialysis vintage, however in some studies dyslipidaemia, disorders of bone mineral metabolism and the use of calcium-based phosphate binders have also been implicated [5,6,10–12,20–25]. Although the presence of diabetes seems to increase the

risk of CAC [14–16] to date no direct comparisons have been reported comparing patients with and without diabetes with the same degree of renal impairment.

The aims of this study were to determine the prevalence and extent of CAC in asymptomatic patients with CKD stages 3 and 4 comparing those with and those without diabetes. We used MSCT to measure CAC scores and examined prognostic factors.

As both MSCT and EBCT are expensive and not always available a further aim of our study was to evaluate the potential of identifying peripheral arterial calcification (PAC) detected in a foot radiograph, as a surrogate marker of CAC.

Subjects and Methods

A cross-sectional study was carried out in both male and female patients with CKD stages 3 and 4, aged between 18–65 years. Two groups were recruited according to diabetes status. Exclusion criteria were known coronary heart disease (CHD), history of angina, myocardial infarction, previous coronary artery revascularization or a positive diagnostic test (stress test, angiography, radionuclide imaging). Patients with a significant arrhythmia, that could preclude gating during the MSCT, were also excluded. A detailed history and physical examination were performed on all participants at inclusion into the study. All patients gave written informed consent, and the local Ethics and Research and Development Committees approved the study protocol. All investigations were performed on the day of the CT scan. Routine biochemistry was performed on a single fasting serum sample collected in the morning and included the following: intact PTH (iPTH), lipid profile (total cholesterol, low and high density protein levels, triglycerides), calcium (adjusted for albumin), phosphate, bicarbonate, albumin and glycated haemoglobin. Urinary calcium and protein: creatinine ratio (UPC) was also determined. The four-variable modification of diet in renal disease (MDRD) equation estimated glomerular filtration rate (eGFR) was used for the determination of CKD stage.

Radiology

Multislice CT scanning of the thorax was performed on a GE (General Electric) Medical Systems Lightspeed 16 scanner to determine coronary artery calcification. The data acquisition parameters were 120 KVp, 350 mA, slice width 2.5 mm, gantry rotation time 0.5 seconds and thick/speed 2.5 mm/8i. Data were reconstructed with a standard algorithm using a 512×512 matrix, 50 cm scan field of view and 25 cm display field of view. The system was synchronized with the cardiac cycle to trigger scanning during the diastolic phase. All pixels with an intensity $\geq$130 Hounsfield units were counted and data were analysed using CardIQ Smart Score software (GE). Calcification score was determined using the Agatston/Janowitz scoring system [26], a score above zero was considered to identify the presence of calcium.

A standardized plain radiograph of the left foot was taken to determine if there was any calcification of the dorsalis pedis artery. Peripheral arterial calcification (PAC) was reported as absent or present. A single radiologist, blinded to the patients' clinical status, reported all the scans and x-rays.

Statistics

All data are presented as mean $\pm$ SD, medians and range, and proportions as appropriate. Student *t*-test was used for continuous variables and Fisher's Exact was used for discrete variables. A significant difference is assumed with P less than 0.05.

The presence or absence of CAC and PAC were analysed as discrete traits. CAC scores were log transformed to allow analysis of severity of CAC.

Significant variables identified by univariate analysis, namely age, gender, diabetes status, eGFR, body mass index (BMI), systolic BP (SBP), smoking history, iPTH, phosphate, bicarbonate and low-density lipoprotein (LDL), were entered into a binary logistic regression analyses (to identify variables associated with presence or absence of CAC) and a multivariate linear regression analysis model (to identify variables associated with severity of CAC). Odds ratio (OR) and 95% confidence interval (95% CI) are reported for logistic regression (goodness of fit evaluated by Homer and Lemeshow test). Adjusted R^2 is reported for multivariate linear analysis (model evaluated by inspecting the normal P-P plot of the regression standardized residuals). The 2×2 table model method of analysis was used to evaluate the diagnostic value of measuring PAC.

All analyses were performed using the Statitical Package for Social Science (SPSS for windows version 14, SPSS Inc, Chicago, IL).

Results

In total, 112 patients were included in the study, 54 with diabetes (median age 53.5 years, 32 males) and 58 without (median age 50 years, 35 males). Ninety-nine percent were Caucasian, 70 patients (33 with diabetes) were CKD stage 3 and 42 patients (21 with diabetes) were CKD stage 4. Primary renal diseases included: diabetic nephropathy (34%), glomerulonephritis (14%), reflux nephropathy (11%), renovascular disease (10%), polycystic kidney disease (10%), vasculitis (4%), other causes (10%) and unknown cause (7%). Baseline clinical characteristics and biochemical parameters for the two groups (with and without diabetes) are shown in Tables 1 and 2 (biochemistry values represent a single fasting measurement). The two groups were well matched for age, gender and most of the clinical characteristics. However, patients with diabetes had significantly higher BMI and SBP and lower total and LDL cholesterol levels. Phosphate, calcium phosphate product and bicarbonate blood levels were all higher in patients with diabetes, and antiplatelet and statin medications were prescribed more frequently to patients with diabetes (Tables 1 and 2).

Table 1. Baseline clinical characteristics of the two groups, *P*-values compare patients with and without diabetes

Variable	Without diabetes	With diabetes	*P*-value
Number	58	54	0.982
Age (years)	50 (26–60)	53.5 (33–65)	0.058
Gender (male: female)	35:23	32:22	0.907
Body mass index (kg/m^2)	27.9 ± 5.4	30.8 ± 5.8	0.010
Family history of premature CHD (yes: no)	2:56	6:48	0.357
Systolic BP (mmHg)	130 ± 16	138 ± 25	0.049
Diastolic BP (mmHg)	79 ± 10	76 ± 15	0.208
Mean arterial pressure (mmHg)	96 ± 10	97 ± 17	0.819
Hypertension diagnosed (yes: no)	55:3	52:2	0.710
Anti-hypertensive medication (yes: no)	54:4	53:1	0.700
Ever smoked (yes: no)	31:27	31:23	0.674
Statins prescribed (yes: no)	21:37	44:10	<0.001
Antiplatelet medication prescribed (yes: no)	13:45	37:17	<0.001
Calcium-based medications prescribed (yes: no)	4:54	9:45	0.335

Table 2. Baseline laboratory data for the two groups, *P*-values compare patients with and without diabetes

Laboratory Variable	Without diabetes $n = 58$	With diabetes $n = 54$	*P*-value
eGFR (ml/min/1.73 m^2)	36 ± 11	36 ± 13	0.926
Adjusted calcium (mmol/l)	2.46 ± 0.09	2.45 ± 0.09	0.277
Phosphate (mmol/l)	1.11 ± 0.25	1.26 ± 0.22	0.002
Calcium phosphate product (mmol/l)	2.74 ± 0.65	3.06 ± 0.58	0.006
Alkaline phosphate (U/l)	188 ± 61	206 ± 200	0.523
Bicarbonate (mmol/l)	24 ± 6	26 ± 3	0.039
iPTH (ng/l)	76 (12–211)	82 (9–451)	0.126
Urinary protein:creatinine ratio (mg/mmol)	70 (10–940)	70 (10–1034)	0.190
Total cholesterol (mmol/l)	5.06 ± 0.98	4.55 ± 1.44	0.029
Triglycerides (mmol/l)	1.89 ± 0.93	2.07 ± 1.26	0.374
HDL (mmol/l)	1.39 ± 0.33	1.31 ± 0.37	0.225
LDL (mmol/l)	2.83 ± 0.94	2.32 ± 1.25	0.022

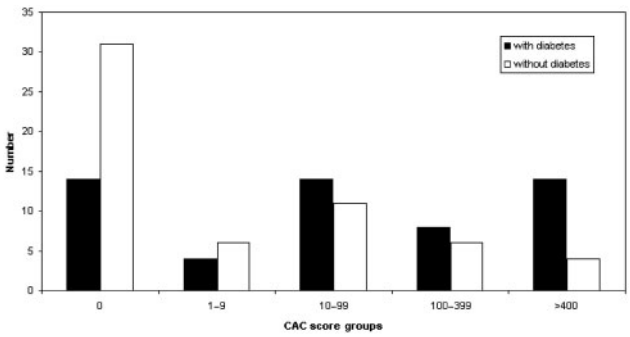

Fig. 1. Distribution of the prevalence of Total CAC group according to diabetes status.

Table 3. Number and sites of calcified arteries comparing the two groups

	Without diabetes ($n = 58$)	With diabetes ($n = 54$)
Number of arteries with calcification		
Single artery	9	5
Two arteries	6	12
Three arteries	6	11
Four arteries	4	7
Five arteries	2	5
Site of arterial calcification		
Left anterior descending	18	38
Right coronary	17	26
Circumflex	12	25
Left main coronary	15	17
Posterior descending	4	9

Coronary artery calcification

CAC was present in 60% of the group as a whole; prevalence was significantly higher in patients with diabetes (74%) compared with those without diabetes (46.6%) ($P = 0.003$). Patients with diabetes also had higher CAC scores ($P = 0.002$) with more vessels affected ($P = 0.03$) (data shown in Figure 1 and Table 3). In the group without diabetes, prevalence of CAC was higher in men than women (60% compared with 26%, $P = 0.003$). Figure 2 and Table 4 shows the distribution of the extent of CAC comparing diabetes status and gender, [median (range) and mean (95% CI for mean)]. Women with diabetes developed calcium deposits at a similar age as the men (Figure 3).

The known duration of diabetes (17.9 ± 11.3 years *vs* 17.7 ± 11.4 years $P = 0.966$) and the level of glycated haemoglobin (8.44 ± 1.66% *vs* 8.96 ± 1.76%, $P = 0.342$) were not different in diabetes subjects with and without CAC.

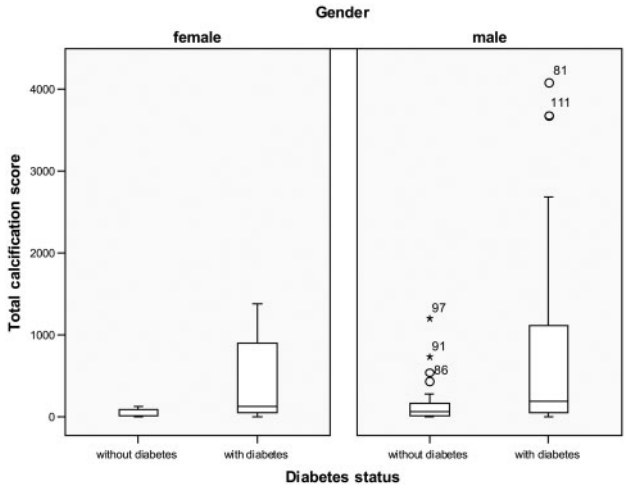

Fig. 2. Box plot of the distribution of Total calcification score by diabetes status and gender.

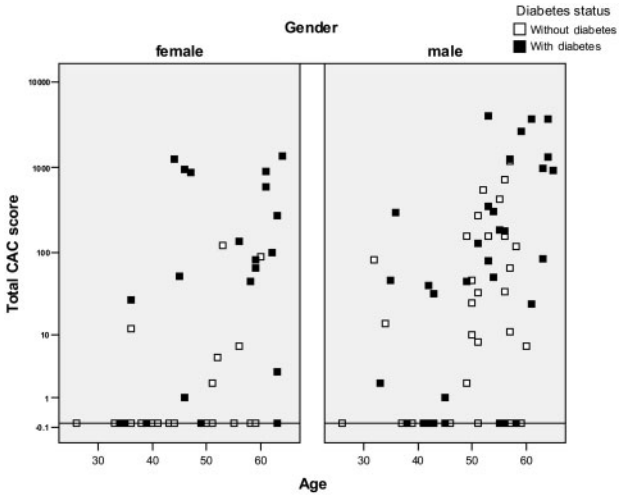

Fig. 3. Total CAC score vs... Age in years described by gender and diabetes status (plotted on logarithmic scale).

Table 4. Supporting data for Figure 2. Mean and 95% CI and median and range CAC scores for female and male subjects with and without diabetes.

	Females		Males	
	Without diabetes	With diabetes	Without diabetes	With diabetes
Median (range)	10 (2 to 120)	118 (1 to 1370)	65 (2 to 1196)	183 (1 to 4074)
Mean (95% CI)	39 (−15 93)	420 (160 679)	194 (57 332)	852 (303 1401)

In the group with diabetes, age was the unique explanatory variable for detecting the presence of CAC (OR = 1.095, 95% CI 1.022, 1.174 ($P = 0.01$). In the same group age and smoking history were the significant predictors for the severity of CAC (Adjusted $R^2 = 0.338$, $P < 0.001$).

In the group without diabetes, the significant predictors for detecting the presence of CAC were age, male gender, BMI, eGFR and serum phosphate levels. The ORs are shown in Table 5 ($P = 0.002$ for the model). In the same group log iPTH was the only variable significantly associated with the severity of CAC (adjusted $R^2 = 0.563$, $P = 0.002$).

For the whole group the significant predictors for detecting the presence of CAC were age (OR: 1.10, 95% CI: 1.05–1.16), diabetes (OR: 2.55, 95% Cl: 1.04–6.26) and BMI (OR: 1.10, 95% CI: 1.02–1.20). Predictors for the severity of CAC were age, diabetes, male gender, smoking history and log iPTH (adjusted $R^2 = 0.300$ $P < 0.001$)

Peripheral artery calcification (PAC)

Peripheral calcification of the dorsal pedis artery was detected in 63% of the patients with diabetes compared with 12% in those without diabetes ($P < 0.001$).

Table 5. Odds ratios estimated from the binary logistic regression model for the prediction of presence of coronary artery calcification, in the patients without diabetes ($n = 58$) P-value for the model <0.002

Variable	B	Standard error	P-value	Odds ratio	95% CI
Age	0.264	0.088	0.003	1.302	1.10–1.55
Male gender	3.778	1.380	0.006	43.713	2.92–654.0
BMI	0.428	0.178	0.016	1.535	1.08–2.18
eGFR	0.102	0.042	0.017	1.107	1.02–1.20
Phosphate	0.581	0.223	0.009	1.788*	1.16–2.76

*for every 0.1 unit change.

The presence of PAC on plain radiograph identified patients with CAC on MSCT, with a sensitivity of 73%, a specificity of 28%, a positive predictive value of 44% and a negative predictive value of 76%. Chi-square analysis of CAC absent/present and PAC absent/present was just significant, $P = 0.044$.

Discussion

This study is the first to compare prevalence rates and severity of CAC in patients with CKD stages 3 and 4 with and without diabetes using MSCT scanning. We report an overall prevalence of CAC of 60% in CKD stage 3 and 4 subjects and when diabetes was present this increased to 74%. Increased prevalence of CAC has been reported previously in several studies of pre-dialysis CKD patients with rates ranging between 27–94% [14–18]. Diabetes has also been shown to be associated with an increased risk of developing CAC in subjects with and without renal disease [15–17,27]. Mehrotra *et al*. [27] reported a CAC prevalence of 93% in patients with diabetic nephropathy compared with

63% in subjects with diabetes without nephropathy; interestingly, in their study both the prevalence and severity of calcification were similar across stages 1 to 5 CKD. In another study of 32 type 2 diabetes patients, with a mean eGFR of 49.8 ± 6.1 ml/min/1.73 m^2, a similar prevalence of CAC (94%) was reported.

No previous study has directly compared CKD patients, with the same degree of kidney failure, with and without diabetes to clarify the relative contribution of diabetes to the presence of CAC in a CKD population. In this cross sectional study, we show that diabetes is clearly a major risk factor for the presence, severity and extent of CAC in subjects with CKD stages 3 and 4. Diabetes status *per se* was strongly predictive of CAC, overshadowing the effect of other risk factors, although it was surprising that the duration of diabetes and the level of diabetic control, as judged by Hb A1c, did not correlate with CAC.

Previous studies have demonstrated a higher risk of CAC in men both with [1,4] and without CKD [28,29] and a similar gender difference has been reported in diabetes, 93% in males compared with 74% in females [27]. In our study, men without diabetes were significantly more likely to have CAC compared with women without diabetes. However the gender difference was lost in patients with diabetes where women were just as likely to have CAC as men; this is in agreement with Merjanian *et al*. [15]. It is known that in men, established coronary heart disease (CHD) is a greater risk factor than diabetes for CHD mortality and this is reversed in women when diabetes carries the greater risk of CHD mortality [30].

In addition to diabetes, other traditional CVD risk factors such as age, obesity, dyslipidaemia, hypertension and smoking have also been associated with CAC. Age is consistently a risk factor for the presence and severity of CAC, both in the general population and in patients with CKD [6,10,11,14,23,31] and we confirm this in our study. In the present study, CAC was detected in relatively young individuals, as previously reported in patients receiving dialysis [6]. Obesity, another established CVD risk factor for CHD [6,14,28,32], was also an independent predictor for the presence of CAC in our non-diabetic group. Colinearity between BMI and diabetes was identified. Dyslipidaemia has been associated with CAC in some studies of end-stage renal disease (ESRD) and in pre-dialysis CKD patients [6,14,20,23], but we could not confirm this relationship. This may be because our patients with diabetes, the group at higher risk for CAC, were more frequently prescribed HMG CoA reductase inhibitors and as a consequence had lower total and HDL cholesterol levels. Hypertension has also been linked to CAC in studies in pre-dialysis and ESRD patients [10,27], but in our study was not an independent predictor of CAC. Smoking correlates with CAC in the general population [33,34] and in the present study was a determinant of the severity of CAC for the group with diabetes.

In addition to the traditional CVD risk factors described above, CAC has also been associated with disorders of calcium and phosphate balance in ESRD populations [6,10,20,23,25]. Interestingly, in our study phosphate levels were found to be an independent predictor for the presence of CAC in patients without diabetes despite the majority of values being within the normal range. This has not been previously reported, although Tomiyama *et al*. [14] reported a correlation between phosphate levels and severity of CAC (the majority of phosphate values within their study group were also within the normal range). Also, the majority of patients in this study were not prescribed calcium-based phosphate binders suggesting that the complications associated with dialysis populations do not apply. We also report that iPTH levels correlated with the extent of CAC in subjects without diabetes but not in patients with diabetes. It may be that diabetes is such a strong risk factor that it overshadows the effect of parathyroid hormone and phosphate.

An additional aim of this study was to determine whether or not a plain radiograph of the foot, to look for vascular calcification, would act as a surrogate marker for the presence of CAC. Our results do not support this since the sensitivity, specificity and predictive values were inadequate for screening purposes. Nevertheless, coexistence of CAC and PAC was common, particularly in subjects with diabetes and CKD.

The results from this investigation should be interpreted while taking into account potential limitations. First, the cross-sectional design, as a prevalence study represents a 'snap shot' of the population studied, and 99% were Caucasian, the findings may not apply to other ethnic groups. Second, single measurements were made of biochemical parameters, rather than time-averaged values. Third, there is the possibility of recall bias (e.g. smoking history) however we feel this would affect both groups equally and we used ever *vs* never to allow for this. Fourth, a number of confounders were identified (e.g. BMI and diabetes); in each case colinearity where co-linearity was identified the variable with the strongest relationship was used in our analysis. Finally, the lack of control populations without CKD and diabetes is a limitation of this study.

In conclusion, we found that CAC is common in patients with CKD stages 3 and 4, particularly in those with diabetes where it affects men and women to the same extent. CAC was also found in relatively young patients, as young as 32 years. Factors such as age, gender and diabetes status are not reversible and although not interventional, our study shows the potential deleterious effect of obesity and smoking on CAC. Further studies are needed to establish precisely when CAC develops in the course of CKD and diabetes, the rate of progression, and whether the process is reversible.

Acknowledgements. We wish to thank the radiology staff at the Nottingham University Hospital, City Campus for their help with the study.

Conflict of interest statement. None declared.

References

1. Budoff MJ, Georgiou D, Brody A *et al*. Ultrafast computed tomography as a diagnostic modality in the study of coronary disease: a multicenter disease. *Circulation* 1996; 93: 898–904
2. O'Rourke RA, Brundage BH, Froelicher VF *et al*. American College of Cardiology/American Heart Association Expert Consensus document on electron beam computed tomography for the diagnosis and prognosis of coronary artery disease. *Circulation* 2000; 102: 126–140
3. Horiguchi J, Yamamoto H, Akiyama Y *et al*. Coronary artery calcium scoring using 16-MDCT and a retrospective ECG-gating reconstruction algorithm. *Am J Roentgenol* 2004; 183: 103–108
4. Wong ND, Budoff MJ, Pio J *et al*. Coronary calcium and cardiovascular event risk: evaluation by age- and sex- specific quartiles. *Am Heart J* 2002; 143: 456–459
5. Oh J, Wunsch R, Turzer M *et al*. Advanced coronary and carotid arteriography in young adults with childhood-onset chronic renal failure. *Circulation* 2002; 106: 100–105
6. Goodman WG, Goldin J, Kuizon BD *et al*. Coronary-artery calcification in young adults with end-stage renal disease who are undergoing dialysis. *N Engl J Med* 2000; 342: 1478–1483
7. Schwarz U, Buzello M, Ritz E *et al*. Morphology of coronary atherosclerotic lesions in patients with end-stage renal failure. *Nephrol Dial Transplant* 2000; 15: 218–223
8. Block GA, Spiegel DM, Ehrlich J *et al*. Effects of sevelamer and calcium on coronary artery calcification in patients new to hemodialysis. *Kidney Int* 2005; 68: 1815–1824
9. Spiegel DM, Raggi P, Mehta R *et al*. Coronary and aortic calcifications in patients new to dialysis. *Hemodialysis Int* 2004; 8: 265–272
10. Braun J, Oldendorf M, Moshage W *et al*. Electron beam computed tomography in the evaluation of cardiac calcification in chronic dialysis patients. *Am J Kidney Dis* 1996; 27: 394–401
11. Moe SM, O'Neill KD, Fineberg N *et al*. Assessment of vascular calcification in ESRD patients using spiral CT. *Nephrol Dial Transplant* 2003; 18: 1152–1158
12. Chertow GM, Raggi P, Chasan-Taber S *et al*. Determinants of progressive vascular calcification in haemodialysis patients. *Nephrol Dial Transplant* 2004; 19: 1489–1496
13. Haydar AA, Hujairi NM, Covic AA *et al*. Coronary artery calcification is related to coronary atherosclerosis in chronic renal disease patients: a study comparing EBCT-generated coronary artery calcium scores and coronary angiography. *Nephrol Dial Transplant* 2004; 19: 2307–2312
14. Tomiyama C, Higa A, Dalboni MA *et al*. The impact of traditional and non-traditional risk factors on coronary calcification in pre-dialysis patients. *Nephrol Dial Transplant* 2006; 21: 2464–2471
15. Merjanian R, Budoff M, Adler S *et al*. Coronary artery, aortic wall, and valvular calcification in nondialyzed individuals with type 2 diabetes and renal disease. *Kidney Int* 2003; 64: 263–271
16. Quinbi WY, Abouzahr F, Mizani MR *et al*. Cardiovascular calcification in Hispanic Americans (HA) with chronic kidney disease (CKD) due to type 2 diabetes. *Kidney Int* 2005; 68: 271–277
17. Kramer H, Toto R, Peshock R *et al*. Association between chronic kidney disease and coronary artery calcification: the Dallas Heart Study. *J Am Soc Nephrol* 2005; 16: 507–513
18. Russo D, Palmiero G, De Blasio AP *et al*. Coronary artery calcification in patients with CRF not undergoing dialysis. *Am J Kidney Dis* 2004; 44: 1024–1030
19. Matsuoka M, Iseki K, Tamashiro M *et al*. Impact of high coronary artery calcification score (CACS) on survival in patients on chronic hemodialysis. *Clin Exp Nephrol* 2004; 8: 54–58
20. Tamashiro M, Iseki K, Sunagawa O *et al*. Significant association between the progression of coronary artery calcification and dyslipidaemia in patients on chronic hemodialysis. *Am J Kidney Dis* 2001; 38: 64–69
21. Rosas SE, Mensah K, Weinstein RB *et al*. Coronary artery calcification in renal transplant recipients. *Am J Transplant* 2005; 5: 1942–1947
22. Splendiani G, Morosetti M, Manni M *et al*. Cardiac calcium evaluation in hemodialysis patients with multisection spiral computed tomography. *Int J Artif Organs* 2004; 2: 759–765
23. McCullough PA, Soman S. Cardiovascular calcification in patients with chronic renal failure: are we on target with this risk factor? *Kidney Int* 2004 Sep; [90]: S18–S24
24. McCullough PA, Sandberg KR, Dumler F *et al*. Determinants of vascular calcification in patients with chronic kidney disease and end stage renal disease: A systematic review. *J Nephrol* 2004; 17: 205–215
25. Chertow GM, Burke SK, Raggi P. Treat to Goal Working Group. Sevelamer attenuates the progression of coronary and aortic calcification in hemodialysis patients. *Kidney Int* 2002; 62: 245–252
26. Agatston AS, Janowitz WR, Hildner FJ *et al*. Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol* 1990; 15: 827–832
27. Mehrotra R, Budoff M, Chrinstenson P *et al*. Determinants of coronary artery calcification in diabetics with and without nephropathy. *Kidney Int* 2004; 66: 2022–2031
28. Wong ND, Kouwabunpat D, Vo AN *et al*. Coronary calcium and atherosclerosis by ultrafast computed tomography in asymptomatic men and women: relation to age and risk factors. *Am Heart J* 1994; 127: 422–430
29. Callister TQ, Raggi P, Cooil B *et al*. Effect of HMG-CoA Reductase Inhibitors on Coronary Artery Disease as Assessed by Electron Beam Computed Tomography. *N Engl J Med* 1998; 339: 1972–1978
30. Natarajan S, Liao Y, Cao G *et al*. Sex differences in risk for CHD mortality associated with diabetes and established coronary heart disease. *Arch Intern Med* 2003; 163: 1735–1740
31. McClelland RL, Chung H, Detrano R *et al*. Distribution of coronary artery calcium by race, gender, and age: results from the Multi-Ethnic Study of Atherosclerosis (MESA). *Circulation* 2006; 113: 30–37
32. Schoenhagen P, Murat Tuzcu E. Coronary artery calcification and end-stage renal disease: vascular biology and clinical implications. *Cleve Clin J Med* 2002; 69 [Suppl 3]: S12–S20
33. La Monte MJ, FitzGerald SJ, Church TS *et al*. Coronary artery calcium score and coronary heart disease events in a large cohort of asymptomatic men and women. *Am J Epidimiol* 2005; 162: 421–429
34. Goel M, Wong ND, Eisenberg H *et al*. Risk factor correlates of coronary calcium as evaluated by ultrafast computed tomography. *Am J Cardiol* 1992; 70: 977–980

Received for publication: 5.2.07
Accepted in revised form: 22.5.07