Management of serum cholesterol and calcium in predialysis phase of chronic kidney disease is important for prevention of aortic calcification after hemodialysis initiation.

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Introduction

Vascular calcification is an important risk factor influencing cardiovascular complications and vital prognosis in chronic kidney disease (CKD)patients. We previously reported that the strict management of PTH and reducing the dose of calcium-containing phosphate binder as far as possible are important, regarding vascular calcification in patients new to hemodialysis (at ERA-EDTA 2013). However, there are no evidence-based clinical practice guidelines for predialysis CKD patients to prevent from vascular calcification.

Objectives

In this study, we evaluated clinical parameters in the predialysis phase of CKD influencing vascular calcification after dialysis initiation.

Methods

- Design: retrospective cohort study
- Patients: among 117 patients who received hemodialysis in our hospital for at least 3 years between July 2004 and June 2010, we selected 63 patients who had been available for follow-up for at least 1 year before dialysis initiation.
- Parameters investigated: age, gender, cause of ESKD, blood pressure, use of statins, mean daily dose of calcium carbonate after hemodialysis initiation and laboratory data as follows, serum albumin, calcium, phosphate, intact PTH, hemoglobin, factor related to lipid.(average level for 1 years before dialysis initiation)
- Outcome: worsening of aortic arch calcification score (AoACS).
- Statistics: multiple logistic regression model was used for analysis of worsening of AoACS. P<0.05 was considered as significant.

Measurement of Aortic arch calcification score (AoACS)
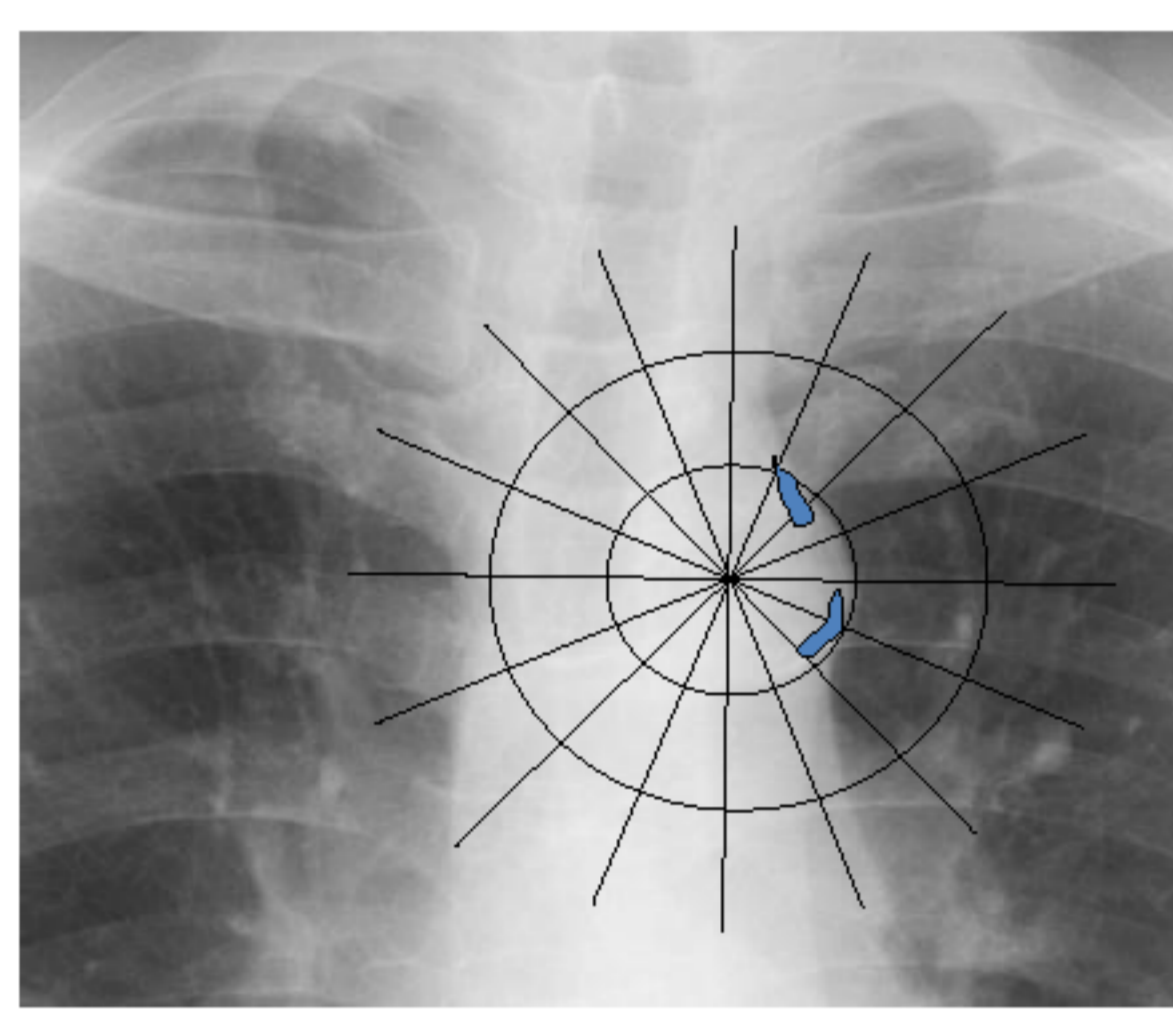
Ogawa et al, Hemodialysis International 2009

1. Use postero-anterior chest X-ray.
2. AoACS is estimated by calcification parts divided 16 x 100 (%)
3. Compare the AoACS score at hemodialysis initiation and 3 years later.
4 Define an outcome as a worsening of AoACS.

Results

Patient's characteristics   n=63

	ratio	mean sd	median (range)
Age		61.3±13.8	62 (31-91)
Gender (M : F)	19:44		
Cause of ESKD DM : non DM	23:40		
Statins (y : n)	13:50		
Average data before hemodialysis initiation			
SBP(mmHg)		144.5±16.9	142 (106 - 212)
DBP(mmHg)		79.8±11.6	78.8 (55 -122)
Albumin (g/dL)		3.6±0.5	3.8 (3.0 - 4.5)
Urea nitrogen (mg/dL)		72.7±17.7	73 (30 - 119)
Cr (mg/dL)		6.6±1.9	6.5 (2.3 - 15.3)
Calcium corrected (mg/dL)		8.2±0.6	8.6 (5.4 - 9.2)
Phosphate (mg/dL)		5.3±0.9	5.3 (3.6 - 8.9)
Ca P (mg^2/dL^2)		43.0±7.7	42.4 (23.2 - 68.7)
Intact PTH (pg/mL)		381.8±366.9	307 (17 - 2600)
Hemoglobin (g/dL)		8.0±1.2	7.9 (5.6 - 11.4)
Total cholesterol (mg/dL)		173.1±43.4	171 (82 - 307)
HDL- cholesterol (mg/dL)		50.7±18.2	47 (18 - 109)
non HDL cholesterol (mg/dL)		118.1±42.0	112 (46 - 242)
Mean daily dose of calcium carbonate **for 3 years after dialysis initiation** (mg/day)		1901±1341	1992 (0 - 5107)

Calcification in aortic arch in 63 cases

	Calcification (+) n (%)	Calcification (-) n (%)
At hemodialysis initiation	29 (46.0)	34 (54.0)
3 years later	49 (77.7)	14 (22.3)

	Worsening n (%)	No change n (%)
Calcification in aortic ach	40 (63.5)	23 (36.5)

Multiple logistic regression analysis

	Univariate analysis			Multivariate analysis		
	Odds ratio	95%CI	p value	Odds ratio	95%CI	p value
Age(every 10y)	1.03	0.70-1.50	0.8945	1.56	0.92-2.74	0.1
Gender(male)	0.52	0.14-1.62	0.2622			
Cause of ESKD (DM)	1.13	0.39-3.37	0.829			
Average data in predialysis phase						
Systolic BP(every 10mmHg)	1.05	0.77-1.46	0.7776			
Diastolic BP(every 10mmHg)	1.00	0.64-1.59	0.9906			
Serum albumin	0.72	0.22-2.08	0.5474	3.14	0.63-17.7	0.1629
Serum Creatinine	0.87	0.64-1.13	0.2954			
Serum corrected calcium	1.88	0.84-4.64	0.128	13.61	3.15-81.1	0.0002
Serum phosphate	0.81	0.45-1.41	0.447			
Ca*P (every 10)	0.98	0.49-1.97	0.9416			
Intact PTH(every 10pg/mL)	1.00	0.98-1.01	0.6528			
Hemoglobin (g/dL)	1.01	0.66-1.57	0.9498			
HDL cholesterol (every 10)	1.00	0.75-1.34	0.9967			
Non HDL cholesterol(every 10)	1.09	0.96-1.26	0.2154	1.24	1.04-1.53	0.0155
Statins	1.38	0.39-5.66	0.6262	3.11	0.68-17.96	0.1491
Average data after hemodialysis initiation						
Mean daily dose of calcium carbonate (every 1000mg)	1.37	0.92-2.10	0.1197	2.65	1.40-5.84	0.0017

Summary

● Forty of the 63 patients reached the outcome.
● Multivariate analysis, using the mean daily dose of calcium carbonate after dialysis initiation and the clinical parameters in predialysis phase of CKD as covariates, identified the mean serum calcium level and non HDL cholesterol level (every 10 mg/dL) as significant independent factors for worsening of the degree of aortic calcification, with odds ratios of 13.6 (95% CI 3.2-81.1) and 1.2 (95% CI 1.04-1.53), respectively.
● On the other hand, no association was observed with the age, presence of diabetes, blood pressure, intact PTH or serum phosphorus level.

Discussion

● Vascular calcification is an important risk factor influencing cardiovascular complications and vital prognosis in chronic kidney disease (CKD)patients.
● Renal function is also associated with worsening of vascular calcification besides diabetes, age, dyslipidemia, level of serum phosphorus and calcium-containing phosphate binder.
● In the view of vascular calcification after dialysis initiation, we demonstrated that lipid management during predialysis CKD phase was important.
● In view of CVD events and mortality, KDIGO's CKD guideline also recommend management of dyslipidemia and the use of statins in adults aged ≥ 50 years with eGFR<60ml/min/1.73mm^2 but not treated with chronic dialysis.
● Although, we were not able to identify the mechanism and type of vascular calcification whether intima calcification, which commonly accompanied with cholesterol plaque, or media calcification, known as Monckebeg-type atherosclerosis, we indicated that management of cholesterol, especially non HDL cholesterol, was important for prevention of vascular calcification, regardless of statins.
● As for serum calcium, calcium overload, such as calcium-containing phosphate binder and activated vitamin D, may accelerate vascular calcification, although vitamin D but not calcium-containing phosphate binder is thought to be better for vital prognosis.

Conclusion

These results suggest that management of non HDL cholesterol and calcium in predialysis phase of CKD is important to prevent vascular calcification after dialysis initiation.

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M) Dialysis. M6) Bone disease in dialysis patients.
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