ism in end-stage renal disease: a UK perspective. *Nephrol Dial Transplant.* 2007;22(5):1428-1436.

47. Mahoney EM, Jurkovitz CT, Chu H, et al. Cost and cost-effectiveness of an early invasive vs conservative strategy for the treatment of unstable angina and non-CT-segment elevation myocardial infarction. *JAMA.* 2002;288(15):1851-1858.

48. Pickard AS, Johnson JA, Feeny DH. Responsiveness of generic health-related quality of life measures in stroke. *Qual Life Res.* 2005;14(1):207-219.

49. Hisashige T, Katayama T, Ishibashi T, et al. Estimation of the quality of the life in patients with diabetes. In: Hisashige T, ed. *Economic Estimation of Healthcare Service by Disease Management, Report on Research on Health Services 2000* [in Japanese]. Tokyo, Japan: Ministry of Health, Labour and Welfare of Japan; 2000:91-98.

50. Hagino H, Nakamura T, Fujiwara S, Oeki M, Okano T, Teshima R. Sequential change in quality of life for patients with incident clinical fractures: a prospective study. *Osteoporos Int.* 2009;20(5):695-702.

51. Garside R, Pitt M, Anderson R, et al. The effectiveness and cost-effectiveness of cinacalcet for secondary hyperparathyroidism in end-stage renal disease patients on dialysis: a systematic review and economic evaluation. *Health Technol Assess.* 2007; 11(18):1-167.

52. Wanner C, Krane V, Marz W, et al. Atorvastatin in patients with type 2 diabetes mellitus undergoing hemodialysis. *N Engl J Med.* 2005;353(2):238-248.

53. Eknoyan G, Beck GJ, Cheung AK, et al. Effect of dialysis dose and membrane flux in maintenance hemodialysis. *N Engl J Med.* 2002;347(25):2010-2019.

54. Cunningham J, Danese M, Olson K, Klassen P, Chertow GM. Effects of the calcimimetic cinacalcet HCl on cardiovascular disease, fracture, and health-related quality of life in secondary hyperparathyroidism. *Kidney Int.* 2005;68(4):1793-1800.

55. Block GA, Zaun D, Smits G, et al. Cinacalcet hydrochloride treatment significantly improves all-cause and cardiovascular survival in a large cohort of hemodialysis patients. *Kidney Int.* 2010;78(6):578-589.

56. Chertow GM, Pupim LB, Block GA, et al. Evaluation of Cinacalcet Therapy to Lower Cardiovascular Events (EVOLVE): rationale and design overview. *Clin J Am Soc Nephrol.* 2007;2(5): 898-905.

57. Messa P, Macário F, Yaqoob M, et al. The OPTIMA Study: assessing a new cinacalcet (Sensipar/Mimpara) treatment algorithm for secondary hyperparathyroidism. *Clin J Am Soc Nephrol.* 2008;3(1):36-45.

58. Fishbane S, Shapiro WB, Corry DB, et al. Cinacalcet HCl and concurrent low-dose vitamin D improves treatment of secondary hyperparathyroidism in dialysis patients compared with vitamin D alone: the ACHIEVE Study results. *Clin J Am Soc Nephrol.* 2008;3(6):1718-1725.

59. Shireman TI, Almehmi A, Wetmore JB, Lu J, Pregenzer M, Quarles LD. Economic analysis of cinacalcet in combination with low-dose vitamin D versus flexible-dose vitamin D in treating secondary hyperparathyroidism in hemodialysis patients. *Am J Kidney Dis.* 2010;56(6):1108-1116.

60. Goodkin DA, Bragg-Gresham JL, Koenig KG, et al. Association of comorbid conditions and mortality in hemodialysis patients in Europe, Japan, and the United States: the Dialysis Outcomes and Practice Patterns Study (DOPPS). *J Am Soc Nephrol.* 2003;14(12):3270-3277.

61. Guideline Working Group, Japanese Society for Dialysis Therapy. Clinical practice guideline for the management of secondary hyperparathyroidism in chronic dialysis patients. *Ther Apher Dial.* 2008;12(6):514-525.

62. Manns B, Meltzer D, Taub K, Donaldson C. Illustrating the impact of including future costs in economic evaluations: an application to end-stage renal disease care. *Health Econ.* 2003; 12(11):949-958.

Clin Exp Nephrol (2011) 15:877–883
DOI 10.1007/s10157-011-0517-y

ORIGINAL ARTICLE

Vascular calcification estimated by aortic calcification area index is a significant predictive parameter of cardiovascular mortality in hemodialysis patients

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Received: 23 April 2011 / Accepted: 26 July 2011 / Published online: 19 August 2011

Abstract

Background Vascular calcification is a feature of arteriosclerosis. In hemodialysis (HD) patients, vascular calcification progresses rapidly. This study used the aortic calcification area index (ACAI), an index of vascular calcification, to evaluate vascular calcification factors in HD patients, to investigate correlations between ACAI and long-term prognosis and to assess correlations between various factors and long-term prognosis.

Methods Subjects comprised 137 patients on maintenance HD. ACAI was measured as an index of vascular calcification as measured by abdominal plain computed tomography. The patients were divided into a high ACAI (H) group and a low ACAI (L) group according to whether the ACAI was below or above the mean value (21.4%) of ACAI, and long-term all-cause death and cardiovascular death rates were compared between groups. Risk factors for all-cause death and cardiovascular death were examined by Cox hazard analysis.

Results During follow-up (mean follow-up period 95.3 ± 50.3 months), 76 patients died, including 46 cardiovascular deaths. Deaths included 51 of 70 patients (67.1%) in Group H and 25 of 67 patients (37.3%) in Group L. Cardiovascular death rates were 51.4 and 14.9%, respectively. On Kaplan–Meier analysis, the number of all-cause deaths was significantly higher in Group H ($P < 0.001$, log-rank test). Similarly, the number of cardiovascular deaths was significantly higher in Group H. Multivariate Cox proportional hazards analysis showed that ACAI (%) was a significant prognostic indicator for cardiovascular death (hazard ratio 1.03; 95% confidence interval 1.00–1.06, $P = 0.03$).

Conclusion High ACAI was clearly correlated with mortality rate in HD patients, particularly cardiovascular mortality rate. ACAI was a useful long-term prognostic indicator in HD patients.

Keywords Abdominal calcification · Hemodialysis · Chronic renal failure · Cardiovascular mortality

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Introduction

In patients with chronic kidney disease (CKD), factors associated with progressive renal dysfunction, including age, hypertension, diabetes, dyslipidemia, and smoking also increase the risk of cardiovascular disease (CVD). In stage 5 hemodialysis (HD) patients, this risk is further

increased. Vascular calcification is closely associated with arteriosclerosis, and in HD patients, even young patients, it progresses at a high rate [1].

Cause of death in about 40% of HD patients involves cardiovascular complications [2]. Vascular calcification is thus a very important issue in terms of prognosis for CKD patients, and evaluation of vascular calcification is essential in daily clinical practice. Recently, to assess vascular calcification, coronary artery calcification has been measured using electron-beam computed tomography (EBCT) and multidetector-row helical CT (MDCT). However, the equipment is expensive, making these investigations difficult to perform in many dialysis facilities. As a vascular calcification index, we have used plain CT, which is available in many facilities, to evaluate abdominal aortic calcification in HD patients using the aortic calcification area index (ACAI); the ACAI is derived from the aortic calcification index (ACI). The ACI is widely used to clinically evaluate abdominal aortic calcification using plain CT [3, 4] and expresses calcification in 12 sectors as a percentage (%), so the extent of calcification in the aortic wall circumference is assessed, but not the thickness. The ACAI directly measures the area of calcification and is a more accurate evaluation of the status of aortic calcification [5]. The present study examined correlations between ACAI and long-term prognosis during a follow-up period of $\geq$10 years. We also examined correlations between various factors and long-term prognosis.

Materials and methods

Subjects

Subjects comprised 137 patients (70 men, 67 women) on maintenance HD at the dialysis center of Ryoushukai Fujii Hospital (Osaka, Japan). Mean age at the time of abdominal CT was 59.7 ± 11.9 years, and mean HD duration was 80.5 ± 64.5 months. Of the 137 patients, 34 (24.8%) had diabetes. HD using hollow-fiber dialyzers was 3 times weekly (4 h/day). Dialysate potassium concentration was 2.0 mEq/L, and calcium concentration was 3.0 mEq/L. Blood flow rate was 200 ml/min, and dialysate flow rate was 500 ml/min. Follow-up period was from January 1996 to July 2008.

Abdominal CT and evaluation of abdominal aortic calcification by ACAI

We used plain CT (SCT-5000TH, Shimadzu, Kyoto, Japan) to evaluate aortic calcification. ACAI was measured as follows: on abdominal plain CT, 10 slices of the abdominal aorta were obtained at 1-cm intervals from bifurcation of the common iliac artery. Aortic cross-sectional area and calcification area were measured using NIH Image software (National Institutes of Health, USA). Calcification area was then divided by cross-sectional area and expressed as a percentage (%). Mean value was calculated for the 10 slices [5].

Biochemical assays and other measurements

Blood tests in each patient were routinely performed before the first weekly hemodialysis session (total of 24 times/1 year). Assays were performed using a standard biochemical analyzer (Auto Biochemical Analyzer 7170, Hitachi, Tokyo, Japan). Systolic and diastolic blood pressures and pulse pressures were measured 156 times/1 year and were shown as mean values in each patient before dialysis.

Statistical methods

Data values were expressed as mean ± SD. The unpaired *t* test, Fisher's test, and chi-squared test were used to compare discrete variables between groups. Survival rates were calculated by Kaplan–Meier analysis. Univariate and multivariate Cox proportional hazard analysis was performed to examine the impact of the baseline levels of ACAI on mortality rate. Multivariate Cox proportional hazard analysis was performed after adjusting for the confounding variables of age, hemodialysis duration, diabetes, systolic hypertension, pulse pressure, lipoprotein a (Lp (a)), using a StatView model (SAS Institute, Cary, NC, USA). The observation period was calculated from the time of CT to the last follow-up date. P values <0.05 were considered statistically significant.

Results

ACAI at baseline

Group H and Group L were defined according to whether the ACAI was above or below the mean value (20.7 ± 15.3%); the group above the mean of ACAI was high (H; mean 33.4 ± 9.5%), and the group below was low (L; mean 7.5 ± 6.1%) (Table 1). Age was significantly higher in Group H than in Group L (64.7 ± 9.9 vs. 54.4 ± 11.6 years; $P < 0.001$). For factors other than age, Group H showed significantly higher systolic blood pressure (148.6 ± 14.7 vs. 138.2 ± 14.7 mmHg; $P < 0.001$), pulse pressure (69.1 ± 11.2 vs. 59.8 ± 12.4 mmHg; $P < 0.001$), serum calcium concentration (9.6 ± 0.4 vs. 9.3 ± 0.4 mg/dL; $P = 0.047$), non-HDL cholesterol (135.6 ± 39.6 vs. 122.6 ± 37.0 mg/dL; $P = 0.049$), Lp

Table 1 Baseline characteristics of hemodialysis patients according to the aortic calcification area index

ACAI (number, mean ± SD)	ACAI high Group (n = 70, mean 33.4 ± 9.5)	ACAI low Group (n = 67, mean 7.5 ± 6.1)	P
Age (years)	64.7 ± 9.9	54.4 ± 11.6	<0.001
Sex (male/female)	41/29	29/38	0.075
Hemodialysis duration (months)	89 ± 65	71 ± 63	0.094
Diabetes mellitus	19 (27.1)	14 (20.9)	0.400
Systolic pressure (mmHg)	149 ± 15	138 ± 15	<0.001
Diastolic pressure (mmHg)	79 ± 9	78 ± 9	0.750
Pulse pressure (mmHg)	69 ± 11	60 ± 12	<0.001
Calcium (mg/dL)	9.6 ± 0.4	9.3 ± 0.4	0.047
Phosphate (mg/dL)	5.2 ± 0.8	5.3 ± 0.9	0.857
Intact PTH (pg/mL)	186 ± 83	196 ± 130	0.609
LDL cholesterol	103 ± 30	95 ± 32	0.153
Non-HDL cholesterol (mg/dL)	136 ± 40	123 ± 37	0.049
Lp (a) (mg/dL)	29 ± 29	19 ± 17	0.019
RAS inhibitor	43 (61.4)	30 (44.8)	0.012
Follow-up duration (months)	79 ± 49	113 ± 46	<0.001
Deaths	51 (67.1)	25 (37.3)	<0.001
Cardiovascular deaths	36 (51.4)	10 (14.9)	<0.001

Values expressed as mean ± SD, number (percent %)

(a) (29.0 ± 29.5 vs. 19.0 ± 17.0 mg/dL; $P = 0.01$) and renin–angiotensin system (RAS) inhibitors [43 (61.4) vs. 30(44.8%); $P = 0.012$].

Patient outcomes

During follow-up (January 1996 to July 2008, mean follow-up period 95.3 ± 50.3 months), 76 patients died. The most common cause was cardiovascular death, occurring in 46 of the 76 patients (Fig. 1). Cardiovascular deaths included ischemic heart failure ($n = 21$, 27%), congestive heart failure ($n = 19$, 25%), and cerebrovascular disease ($n = 6$, 8%). Noncardiovascular deaths included infectious disease ($n = 8$, 11%), malignancy ($n = 5$, 7%), and others [hepatic insufficiency ($n = 4$), accidental deaths ($n = 4$), suicide ($n = 1$) and unknown-deaths ($n = 13$)] ($n = 22$, 22%). Deaths included 51 of 70 patients (67.1%) in Group H and 25 of 67 patients (37.3%) in Group L. Cardiovascular deaths were 36 (51.4%) and 10 (14.9%), respectively (Table 1).

Kaplan–Meier analysis

All-cause deaths and cardiovascular deaths in Group H and Group L were examined by Kaplan–Meier analysis (Fig. 2). Figure 2a shows the difference in the survival curve between ACAI Group H and Group L with regard to all-cause deaths, and Fig. 2b shows the difference with regard to cardiovascular deaths. The number of all-cause deaths was significantly higher in Group H than in Group L ($P < 0.001$). Similarly, Group H showed a significantly higher number of cardiovascular deaths than Group L ($P < 0.001$).

Univariate analysis with Cox proportional hazards models

Table 2 shows univariate Cox hazard analysis of various factors and mortality rate. Age, HD duration, diabetes, systolic blood pressure, and pulse pressure, together with ACAI, were significant prognostic factors for all-cause death; and age, HD duration, diabetes, systolic blood pressure, pulse pressure, Lp (a), together with ACAI, were significant prognostic factors for cardiovascular death.

Multivariate analysis with Cox proportional hazards models

Table 3 shows multivariate Cox hazard analysis of various factors and mortality rate. Multivariate Cox hazard analyses were performed with results from univariate analysis to identify factors associated with mortality. In multivariate analyses, factors that showed P <0.05 on univariate analysis were enrolled as possible factors associated with mortality. Age and HD duration were significant factors associated with all-cause mortality; ACAI was not significant (hazard ratio (HR) 1.02; 95% confidence interval (CI) 0.99–1.04; $P = 0.17$). However, the ACAI was a significant factor associated with cardiovascular mortality (HR 1.03; 95% CI 1.00–1.06; $P = 0.03$) after adjustment for age, HD duration, diabetes, systolic pressure, pulse pressure and Lp (a).

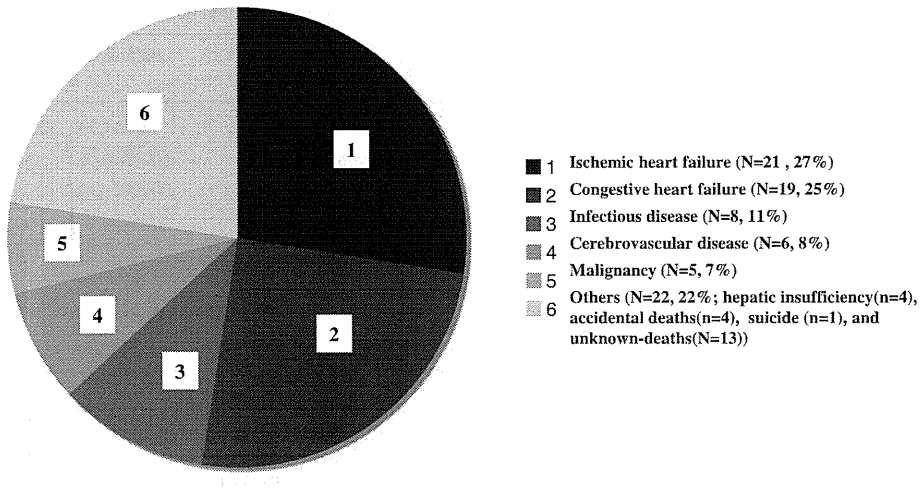

Fig. 1 Causes of death of 76 hemodialysis patients. Cardiovascular deaths included death from ischemic heart failure ($n = 21$), congestive heart failure ($n = 19$), and cerebrovascular disease ($n = 6$); noncardiovascular deaths consisted of infectious disease ($n = 8$), malignancy ($n = 5$), and others ($n = 22$). The study period was from January 1996 to July 2008

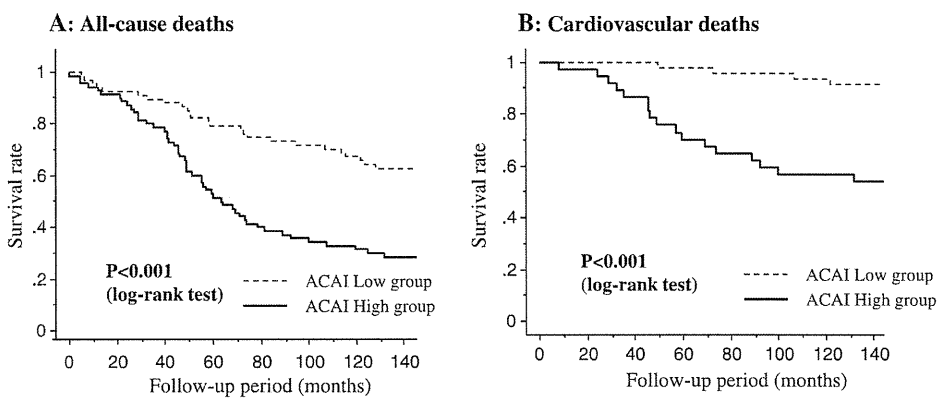

Fig. 2 Kaplan–Meier analysis of all-cause (**a**) and cardiovascular (**b**) deaths of 137 hemodialysis patients. Patients with high ACAI show higher death rate from both all causes and cardiovascular diseases than those with low ACAI (log-rank test, $P < 0.0001$ and $P < 0.0001$). The study period was from January 1996 to July 2008

Table 2 Univariate Cox proportional hazards analysis of factors associated with all-cause and cardiovascular death in hemodialysis patients

	All-cause death			Cardiovascular death		
	Hazard ratio	95% CI	*P*	Hazard ratio	95% CI	*P*
Age (/1 year)	1.11	1.09–1.14	<0.001	1.13	1.09–1.17	<0.001
Sex (male vs. female)	1.33	0.85–2.09	0.22	1.48	0.84–2.62	0.18
Hemodialysis duration (/1 year)	0.94	0.90–0.98	0.01	0.94	0.89–1.00	0.03
Diabetes (diabetes vs. no diabetes)	1.87	1.15–3.02	0.01	2.24	1.26–4.00	0.01
Systolic pressure (/1 mmHg)	1.02	1.00–1.03	0.02	1.03	1.01–1.05	0.01
Diastolic pressure (/1 mmHg)	0.99	0.96–1.02	0.52	0.99	0.96–1.03	0.66
Pulse pressure (/1 mmHg)	1.03	1.01–1.05	<0.001	1.04	1.02–1.06	<0.001
Calcium (/1 mg/dL)	0.80	0.62–1.04	0.10	0.8	0.57–1.12	0.19
Phosphate (/1 mg/dL)	0.98	0.73–1.31	0.89	0.95	0.66–1.36	0.76
Intact PTH (/1 pg/mL)	1.00	0.99–1.01	0.85	1.00	0.99–1.01	0.68
LDL cholesterol (/1 mg/dL)	1.00	1.00–1.01	0.44	1.01	1.00–1.02	0.12
Non-HDL cholesterol (/1 mg/dL)	1.00	0.99–1.01	0.35	1.01	0.99–1.01	0.18
Lp (a) (/1 mg/dL)	1.01	1.00–1.01	0.05	1.01	1.00–1.02	0.01
RAS inhibitor (no: 0 yes: 1)	1.00	0.63–1.57	0.99	1.20	0.68–2.12	0.53
ACAI (%)	1.04	1.02–1.05	<0.001	1.05	1.03–1.07	<0.001

Table 3 Multivariate Cox proportional hazards analysis of factors associated with all-cause and cardiovascular death in hemodialysis patients

	All-cause death			Cardiovascular death		
	Hazard ratio	95% CI	*P*	Hazard ratio	95% CI	*P*
Age (/1 year)	1.11	1.08–1.15	<0.001	1.15	1.10–1.20	<0.001
Hemodialysis duration (/1 year)	0.92	0.87–0.98	0.01	0.94	0.87–1.02	0.14
Diabetes (diabetes vs. no diabetes)	1.26	0.68–2.33	0.46	1.43	0.70–2.90	0.32
Systolic pressure (/1 mmHg)	1.01	0.99–1.03	0.46	1.02	0.98–1.06	0.33
Pulse pressure (/1 mmHg)	1.00	0.96–1.04	0.89	1.01	0.96–1.04	0.81
Lp (a) (/1 mg/dL)	1.00	0.99–1.01	0.79	1.01	1.00–1.06	0.29
ACAI (%)	1.02	0.99–1.04	0.17	1.03	1.00–1.06	0.03

Discussion

Mild renal dysfunction and urinary abnormalities have recently been discovered as strong risk factors for CVD [6]. In HD patients, risk of CVD is 5- to 20-times higher than in the general population, primarily due to early arteriosclerosis [7]. As mentioned previously, vascular calcification has often been reported in HD patients, even at a young age. As indices of vascular calcification in HD patients, aortic arch or common iliac calcification on plain radiographs [8, 9], ACI [3, 4], and EBCT [10] or MDCT [11] have been applied to evaluate coronary artery calcification.

Each of these modalities offers various advantages and disadvantages in terms of convenience, accuracy, and safety. EBCT and MDCT are excellent for quantitative evaluation of coronary artery calcification, but because of the expensive equipment required, are not widely available at many dialysis facilities. Evaluation based on radiographic findings is the most convenient and inexpensive method, and correlations with prognosis have been reported in several reports to date [12, 13]. However, the lack of quantitative evaluation and difficulty of assessing changes over time are still drawbacks.

Plain CT is available even in small and mid-size dialysis centers and is necessary to screen for renal cell carcinoma in HD patients. The advantage is that renal cancer screening and measurement of abdominal aortic calcification can be performed simultaneously. ACAI is a further development of the ACI, which has conventionally been used as an index of abdominal aortic calcification [3, 4]. ACAI provides a more accurate evaluation of calcification in patients with thick calcification, and is also useful to evaluate increases in calcification over time.

The results of our comparison between Group H and Group L showed that systolic blood pressure, pulse pressure, serum calcium concentration, non-HDL cholesterol, Lp (a) concentration and RAS inhibitors, in addition to age, were significantly higher in Group H than in Group L. In 2003, the "Guideline for bone metabolism and disease in chronic kidney disease" by the United States Kidney Disease Outcome Quality Initiative recommended a maximum calcium intake of 1500 mg/day from calcium-containing phosphate binders, widely used as phosphate-binding agents [14]. The goal was prevention of hypercalcemia and excess calcium intake, in light of reports stating that hypercalcemia and excess calcium intake could cause vascular calcification, and that hyperphosphatemia combined with hypercalcemia further increased cardiovascular and mortality risk. Based on these reports, the availability of non-calcium-containing phosphate binders has continued to increase.

Serum levels of calcium, phosphorus and/or intact parathyroid hormone (PTH) levels have been reported to be associated with high levels of CVD morbidity and mortality in patients with end-stage renal disease [15–17]. In this study, serum levels of calcium, phosphate and intact PTH were not associated with cardiovascular mortality. We think the reasons may be as follows. First, when this study was performed, the only available phosphate binder was calcium carbonate, because non-calcium-containing phosphate binders were not available in Japan. Furthermore, the only treatment for secondary hyperparathyroidism was vitamin D agents. Therefore, serum levels of calcium might be high to maintain serum phosphate levels (Group H 9.6 ± 0.4, Group L 9.3 ± 0.4 mg/dL). Furthermore, there were no differences between the two groups with regard to serum levels of intact PTH (Group H 186 ± 83 vs. Group L 196 ± 130 pg/mL; $P = 0.609$). Second, the serum levels of phosphate in the two groups were good control levels and there were no differences between the two groups (Group H 5.2 ± 0.8 vs. Group L 5.3 ± 0.9 mg/dL; $P = 0.857$).

This study evaluated prognostic indicators over a long-term follow-up period of ≥10 years. The most frequent cause of death was cardiovascular death, accounting for 60% of all mortality. Given the long-term evaluation of ≥10 years, age was expected to be a factor with considerable influence. However, on Kaplan–Meier analysis, a high ACAI significantly increased the number of both all-cause deaths and cardiovascular deaths. Univariate Cox hazard analysis showed that age, HD duration, diabetes, systolic blood pressure, pulse pressure, and ACAI were

significant prognostic factors in all-cause death, and that age, HD duration, diabetes, systolic blood pressure, pulse pressure, Lp (a) concentration, and ACAI were significant prognostic factors in cardiovascular death. Ultimately multivariate Cox hazard analysis showed age and HD duration as independent prognostic factors in all-cause deaths. Diabetes, systolic blood pressure, pulse pressure, Lp (a) and ACAI were not significant. But in cardiovascular deaths, age and ACAI were prognostic factors. Our findings suggest that ACAI may be a very useful prognostic indicator for cardiovascular mortality.

Medial calcification is not necessarily associated with lumen stenosis, but because vessel stiffness increases, vascular compliance is decreased [18]. Several mechanisms may explain the association between aortic stiffness and CVD [19]. The arterial stiffness leads to early wave pressure, a decrease of diastolic blood pressure, and a consequent increase of pulse pressure [20]. This increases systolic blood pressure and afterload on the heart, causes left ventricular hypertrophy, and increases myocardial-oxygen demand [21]. In addition, because myocardial blood supply depends largely on pressure throughout diastole and the duration of diastole, the decrease of diastolic blood pressure can compromise coronary perfusion [22]. ACAI as a prognostic factor in cardiovascular death, as demonstrated by our study, may be related to these underlying mechanisms.

We previously published the ACAI method [4]. The ACAI provides a more accurate evaluation of calcification than ACI. However, our study evaluated the relationship between the ACAI measured at one time and future prognosis. In the future, factors leading to serial increases in ACAI, and the influence of these serial increases on prognosis, should be investigated.

Conclusion

Our evaluation of prognosis in 137 HD patients over a period of $\geq$10 years found that the most common cause of mortality was cardiovascular death. In HD patients, ACAI, as measured by abdominal plain CT, was useful as a significant predictive parameter of cardiovascular mortality.

Acknowledgment This work was supported in part by the Grant-in-Aid from the Japanese Society for the Promotion of Science (20590982, 23591222 to T.S.), and by the Public Welfare Science Research Funds (22141101 to T.S.).

References

1. Goodman WG, Goldin J, Kuizon BD, Yoon C, Gales B, Sider D, et al. Coronary-artery calcification in young adults with end-stage renal disease who are undergoing dialysis. N Engl J Med. 2000;18:1478–83.
2. Nakai S, Masakane I, Akiba T, Iseki K, Watanabe Y, Itami N, et al. Overview of regular dialysis treatment in Japan (as of 31 December 2005). Ther Apher Dial. 2007;11:411–41
3. Yukawa S, Sonobe M, Yukawa A, Mimura K, Mune M, Maeda H, et al. Prevention of aortic calcification in patients on hemodialysis by long-term administration of vitamin E. J Nutr Sci Vitam. 1992;38(Suppl):S187–90.
4. Taniwaki H, Ishimura E, Tabata T, Tsujimoto Y, Shioi A, Shoji T, et al. Aortic calcification in haemodialysis patients with diabetes mellitus. Nephrol Dial Transpl. 2005;20(11):2472–8.
5. Ohya M, Otani H, Kimura K, Saika Y, Yukawa S, Shigematsu T, et al. Improved assessment of aortic calcification in Japanese patients undergoing maintenance hemodialysis. Intern Med. 2010;49(19):2071–5.
6. Go AS, Chrtow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med. 2004;351:1296–305.
7. Foley R, Parfrey PS, Sarnak MJ. Clinical epidemiology of cardiovascular disease in chronic renal disease. Am J Kidney Dis. 1998;32(Suppl):S112–9.
8. Shigematsu T, Kono T, Satoh K, Yokoyama K, Yoshida T, Hosoya T, et al. Phosphate overload accelerates vascular calcium deposition in end-stage renal disease patients. Nephrol Dial Transpl. 2003;18(Suppl 3):iii86–9.
9. London GM, Guerin AP, Marhais SJ, Metivier F, Pannier B, Adda H. Arterial media calcification in end-stage renal disease: impact on all-cause and cardiovascular mortality. Nephrol Dial Transpl. 2003;18:1731–40.
10. Raggi P, Boulay A, Chasan-Taber S, Amin N, Dillon M, Burke SK, et al. Cardiac calcification in adult hemodialysis patients. A link between end-stage renal disease and cardiovascular disease? J Am Coll Cardiol. 2002;39:695–701.
11. Yokoyama K, Nishioka M, Sakuma T, Yoshida S, Iida R, Yoshida H, et al. Most patients with coronary artery calcification have no coronary artery stenosis and hyperphosphatemia should be important in reevaluating the K/DOQI guideline. Ther Apher Dial. 2006;10:101.
12. Okuno S, Ishimura E, Kitatani K, Fujino Y, Kohno K, Maeno Y, et al. Presence of abdominal aortic calcification is significantly associated with all-cause and cardiovascular mortality in maintenance hemodialysis patients. Am J Kidney Dis. 2007;49(3):417–25.
13. Ogawa T, Ishida H, Akamatsu M, Matsuda N, Fujiu A, Ito K, et al. Progression of aortic arch calcification and all-cause and cardiovascular mortality in chronic hemodialysis patients. Int Urol Nephrol. 2010;42(1):187–94.
14. K/DOQI Workgroup. Clinical practice guideline for bone metabolism and disease in chronic kidney disease. Am J Kidney Dis. 2003;42(3):S62–84.
15. Qunibi WY. Consequences of hyperphosphatemia in patients with end-stage renal disease (ESRD). Kidney Int Suppl. 2004;90:S8–12.
16. Tonelli M, Sacks F, Pfeffer M, et al. Relation between serum phosphate level and cardiovascular event rate in people with coronary disease. Circulation. 2005;112:2627–33.
17. Mathew S, Tustison KS, Sugatani T, et al. The mechanism of phosphorus as a cardiovascular risk factor in CKD. J Am Soc Nephrol. 2008;19:1092–105.
18. Guerin AP, London GM, Marchais SJ, Metivier F. Arterial stiffening and vascular calcification in end-stage renal disease. Nephrol Dial Transpl. 2000;15:1014–21.
19. Mattace-Raso FU, van der Cammen JM, Hofman A, van Popele NM, Bos ML, Schalekamp MADH, et al. Arterial stiffness and risk of coronary heart disease and stroke: the Rotterdam Study. Circulation. 2006;113:657–63.

20. London GM. Large arteries hemodynamics: conduit versus cushioning function. Blood Press Suppl. 1997;2:48–51.
21. Westerhof N, O'Rourke MF. Haemodynamic basis for the development of left ventricular failure in systolic hypertension and for its logical therapy. J Hypertens. 1995;13:943–52.
22. Watanabe H, Ohtsuka S, Kakihana M, Sugishita Y. Coronary circulation in dogs with an experimental decrease in aortic compliance. J Am Coll Cardiol. 1993;21:1497–506.