Original Article

Plasma Aldosterone in Hypertensive Patients on Chronic Hemodialysis: Distribution, Determinants and Impact on Survival

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A high plasma aldosterone concentration (PAC) is known to be associated with poor outcome in patients with cardiac disease. However, the prognostic value of PAC in chronic hemodialysis (HD) patients is unknown. In 1996 we examined 128 hypertensive patients treated with antihypertensive drugs, excluding angiotensin-converting enzyme inhibitors, who were undergoing chronic HD (ages 61.8±13.8 years, 62% male), and for whom PAC (ng/dl) data were obtained. We followed up these patients until November 2003. During the follow-up period, 30 patients died. About half of all patients (48%) had PAC values above the normal range. We assigned the 128 patients to a lower (<22.9) or higher (≥22.9) PAC group according to the median baseline PAC. The survival rate as calculated by the Kaplan-Meier method was 90.6% in the higher PAC group and 62.5% in the lower PAC group (p=0.003). In multivariate analysis, serum potassium and plasma renin activity were independent determinants of PAC. Cox proportional hazards analysis, with adjustment for other variables including diabetes, showed that lower PAC was independently predictive of death. The adjusted hazard ratio (95% confidence interval) of the lower PAC group was 2.905 (1.187–7.112, p=0.020). The significance of PAC became marginal by adjustment with albumin or potassium. These results indicate that higher PAC is common, but not associated with an increase in total and cardiovascular deaths among hypertensive patients undergoing chronic HD. The association between lower PAC and poor survival may be driven by volume retention and/or lower potassium. (*Hypertens Res* 2006; 29: 597–604)

***Key Words*: aldosterone, renal dialysis, mortality, cardiovascular disease, renin-angiotensin system**

Introduction

The renin-angiotensin-aldosterone system (RAAS) has been shown to play an important role in the pathogenesis of cardiovascular disease (*1*). Although angiotensin II is recognized as the most relevant factor of the system (*2*), aldosterone also contributes to cardiovascular injury, which results in a poor outcome (*3–6*). Moreover, it has been reported that the angiotensin II blockade was not always sufficient to prevent organ damage in patients with a defect of suppression of plasma aldosterone level, and adding aldosterone blockade could be beneficial under this condition (*7*). However, the clinical relevance of aldosterone in chronic hemodialysis (HD) patients, a group at high risk of cardiovascular death (CVD) (*8*), remains to be determined. Hypertension is a frequent complication of chronic HD patients. Schlaich *et al*. (*9*) reported that inadequate aldosterone suppression after high salt intake correlated with left ventricular alterations, even in patients with mild hypertension. It has also been suggested that aldosterone exerts adverse effects on the heart, particularly under conditions of sodium loading (*10–12*). Therefore, aldosterone may

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Table 1. Characteristics of Study Subjects According to Baseline Plasma Aldosterone Concentration (PAC)

Variable	All subjects (n=128)	Lower PAC (n=64)	Higher PAC (n=64)	p value
Female/male sex	49/79	26/38	23/41	n.s.
Age (years)	61.8±13.8	65.8±14.0	57.7±12.5	<0.001
HD duration (m)	82.4±61.2	77.1±64.6	87.7±57.6	n.s.
BMI (kg/m^2)	22.2±3.3	21.9±3.1	22.5±3.5	n.s.
Diabetes (n (%))	29 (22.7)	22 (34.4)	7 (12.3)	0.001
SBP (mmHg)	150.5±17.4	150.8±18.2	150.3±16.7	n.s.
DBP (mmHg)	77.7±10.3	75.5±10.2	79.8±10.0	0.018
Interdialytic BW gain	2.4±0.9	2±1.0	2.7±0.8	<0.001
%BW reduction	4.1±1.5	3.7±1.7	4.6±1.3	0.002
Kt/V	1.1±1.5	1.1±0.2	1.2±0.4	n.s.
CTR	52.4±4.9	52.8±4.8	52±4.9	n.s.
PRA (ng/ml/h)	1.8 (0.2–57.2)	1.1 (0.2–24.1)	3.4 (0.2–57.2)	0.006
PAC (ng/dl)	22.9 (1.3–665)	8.3 (1.3–22.6)	63.4 (23.2–665)	<0.001
Albumin (g/dl)	3.9±0.4	3.8±0.4	4±0.3	<0.001
Tcho (mg/dl)	167.9±36.9	162.6±30.9	167.9±38.4	n.s.
Potassium (mEq/l)	5.2±0.8	5±0.8	5.4±0.7	0.026
Hemoglobin (g/dl)	9.6±1.2	9.6±1.3	9.5±1.1	n.s.
History of MI (n (%))	5 (3.9)	2 (3.1)	3 (4.7)	n.s.
History of stroke (n (%))	14 (10.9)	6 (9.4)	8 (12.5)	n.s.
ASO (n (%))	9 (7.0)	5 (7.8)	4 (6.3)	n.s.

HD, hemodialysis; BMI, body mass index (calculated with pre-dialysis body weight); SBP, systolic blood pressure, pre-dialysis; DBP, diastolic blood pressure, pre-dialysis; BW, body weight; %BW reduction, % body weight reduction per session; CTR, cardiothoracic ratio; PRA, plasma renin activity; PAC, plasma aldosterone concentration; Tcho, total cholesterol; MI, myocardial infarction; ASO, atherosclerosis obliterans; n.s., not significant; lower PAC, <22.9 ng/dl; higher PAC, ≥22.9 ng/dl. Data are expressed as means±SD or n (%) except for PRA and PAC, which are expressed as medians (range).

play a significant role in the pathogenesis of cardiovascular disease in chronic HD patients, who generally suffer from chronic sodium retention. In accordance with this hypothesis, Sato *et al*. (*13*) reported that aldosterone is associated with left ventricular hypertrophy in nondiabetic (non-DM) patients undergoing chronic HD. To our knowledge, there are no studies on the role of aldosterone in the prognosis of chronic HD patients. To elucidate the prognostic value of aldosterone, we examined the distribution of the plasma aldosterone concentration (PAC) and its determinants in hypertensive patients undergoing chronic HD. We then assessed the association between baseline PAC and survival.

Methods

Subjects

Of 221 chronic HD patients at Okinawa Dai-ichi Hospital, Okinawa, Japan, we examined the plasma renin activity (PRA) and PAC of all 154 hypertensive patients treated with antihypertensive drugs in 1996. After excluding subjects treated with angiotensin-converting enzyme inhibitors (angiotensin II receptor blocker was not commercially available in Japan in 1996), we studied 128 hypertensive patients. The subjects, 79 men (62%) and 49 women (38%), were retrospectively reviewed for death, renal transplantation, or transfer to another clinic from March 1, 1996, to November 30, 2003. The patients were undergoing 2 or 3 sessions of HD a week for 3–5 h per session.

Baseline Data

PRA, PAC, and other baseline laboratory and clinical data were obtained prior to routine HD at the start of the week with 2 or 3 days' interdialytic interval. Predialysis blood samples for measurement of PRA and PAC were obtained after the patients had rested in the supine position for at least 15 min. PRA was measured with a commercial radioimmunoassay kit (Renin-Riabead; Abbott Japan Co., Ltd., Tokyo, Japan). PAC was measured with a commercial radioimmunoassay kit (SPAC-S Aldosterone; Dai-ichi Radioisotope Laboratory Co., Ltd., Tokyo, Japan) with a sensitivity of less than 1 ng/dl. The SPAC-S Aldosterone kit has an intraassay coefficient of variation range from 1.8% at high levels to 8.3% at low levels with corresponding interassay coefficients of variation ranging from 2.4% to 3.2%. Body mass index (BMI) was defined as the ratio of weight to height squared (kg/m^2).

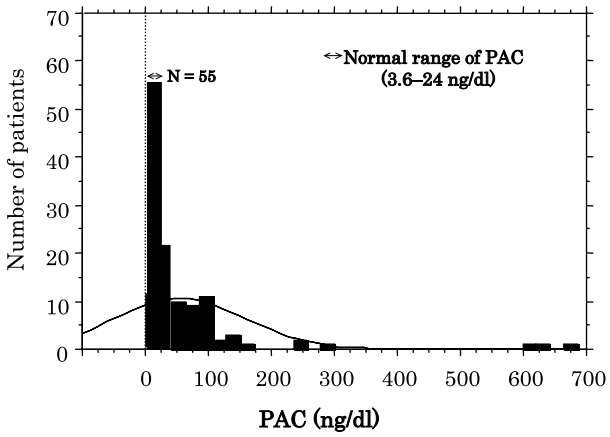

Fig. 1. *Distribution of the baseline plasma aldosterone concentration (PAC).*

Cause of Death

Cause of death was noted as cardiovascular (acute myocardial infarction, heart failure, stroke, sudden death) or non-cardiac (infection, malignancy, withdrawal).

Statistical Analysis

The unpaired *t*-test and the χ^2 test were used to analyze differences in discrete variables between the groups. Survival curves were calculated by the Kaplan-Meier method. Cox proportional hazards analysis was performed to examine the significance of baseline PAC as a predictor of outcome after adjusting for confounding variables using SAS software (SAS Institute, Cary USA). Determinants of baseline PAC were examined by multivariate logistic analysis. The Tukey-Kramer test was used to analyze the differences in subgroup analysis based on the median value of potassium and PAC in non-DM patients. Data are expressed as the means (SD or SEM). *p* values less than 0.05 were considered statistically significant.

Results

Study Subjects and Deaths

The characteristics of the study subjects are summarized in Table 1. During the 7-year-follow-up period, 30 (23.4%) study patients died, including 9 whose deaths were attributed to a cardiovascular event. Two patients underwent renal transplantation, and two others transferred out of our dialysis unit. Cardiovascular causes of death included cardiac arrest, cardiac arrhythmia, myocardial infarction, stroke, and sudden death. Noncardiac causes of death included infection, such as sepsis or pneumonia, malignancy, withdrawal, and unknown causes.

PRA and PAC Distributions

Figure 1 shows the distribution of the PAC baseline. PAC values ranged between 1.3 and 665 ng/dl (mean, 54.9±103.3 ng/dl; median, 22.9 ng/dl). About half of the patients (N=61, 47.7%) had PAC above the normal range of 3.6–24 ng/dl at the supine position, and 43% of the patients were within the normal range. The PAC distribution was not symmetrical, so we divided the study subjects into two groups, a higher PAC (≥22.9 ng/dl) and a lower PAC (<22.9 ng/dl) group, according to the median baseline PAC, in order to study the relationship between PAC and outcome. In the patients with an extremely high value of PAC, secondary hypertension was ruled out by additional examinations.

Baseline Characteristics of Study Subjects

Compared to the higher PAC group, the lower PAC group showed significantly greater age, greater incidence of diabetes (DM), lower diastolic blood pressure (DBP), lower percent reduction in body weight (BW) per one HD session (%BW reduction), lower PRA, lower serum albumin level, and lower serum potassium level (Table 1). We guided the restriction of sodium intake (less than 5 g/day) for all patients. This guidance seemed to have a substantial effect, since the %BW reduction was less than 5%. Although the lower PAC group showed a lower %BW reduction per session, the cardiothoracic ratio (CTR) did not differ significantly between the two groups. There were no significant differences in the incidence of past history of cardiovascular disease or the level of serum calcium or serum phosphate between the groups (data not shown).

Survival Rate and Cause of Death Relative to Baseline PAC

Survival curves stratified by baseline PAC are shown in Fig. 2. The 7-year-survival rates were 90.6% in the higher PAC group and 62.5% in the lower PAC group. The survival rate was significantly lower in the lower PAC group than in the higher PAC group.

The causes of death are shown in Table 2. All-cause, cardiovascular, and non-cardiovascular mortalities were significantly higher in the lower PAC group than in the higher PAC group: the latter had only 2 cases of CVD.

Determinants of PAC

The determinants of PAC were evaluated by multivariate logistic regression analysis (Table 3). Serum potassium and the logarithm of PRA were significant determinants of PAC. The presence of diabetes was associated with lower PAC, although the association did not reach the level of statistical significance.

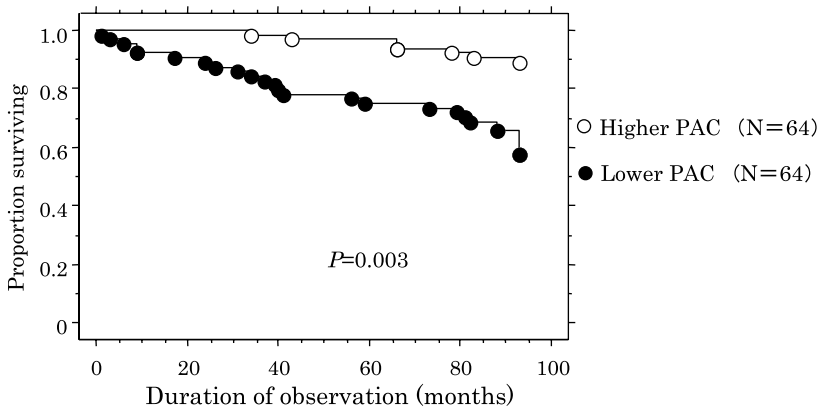

Fig. 2. *Survival curves based on the baseline plasma aldosterone concentration (PAC). Higher PAC, ≥22.9 ng/dl; lower PAC, <22.9 ng/dl.*

Table 2. Cause of Death According to Baseline Plasma Aldosterone Concentration (PAC)

Cause of death	All (n=128)	Lower PAC (n=64)	Higher PAC (n=64)	p value
All causes (n (%))	30 (23.4)	24 (37.5)	6 (9.4)	
Cardiovascular (n (%))	9 (7.0)	8 (12.5)	1 (1.6)	0.001
MI or CHF	4 (3.1)	3 (4.7)	1 (1.6)	
Stroke	2 (1.6)	2 (3.1)	0 (0.0)	
Sudden death	3 (2.3)	3 (4.7)	0 (0.0)	
Non-cardiovascular (n (%))	21 (16.4)	16 (25)	5 (7.8)	0.001
Infection	14 (10.9)	12 (18.8)	2 (3.1)	
Malignancy or withdrawal	4 (3.1)	3 (4.7)	1 (1.6)	
Other	3 (2.3)	1 (1.6)	2 (3.1)	

MI, myocardial infarction; CHF, congestive heart failure; lower PAC, <22.9 ng/dl; higher PAC, ≥22.9 ng/dl.

Table 3. Determinants of Higher Baseline Plasma Aldosterone Concentration (PAC) by Multivariate Logistic Analysis

Variable	Odds ratio	95% CI	p value
Male *vs*. female sex	0.824	0.295–2.306	n.s.
Age (years)	0.971	0.934–1.009	n.s.
HD duration (months)	1.002	0.994–1.009	n.s.
BMI (kg/m^2)	1.158	0.995–1.348	n.s.
Diabetes	0.359	0.103–1.249	n.s.
%BW reduction	1.439	0.996–2.080	n.s.
Serum albumin (g/dl)	1.346	0.280–6.464	n.s.
Potassium (mEq/l)	2.163	1.053–4.443	0.036
Logarithm PRA	14.601	4.373–48.740	<0.001

CI, confidence interval. Other abbreviations are explained in the first footnote in Table 1.

PAC and Survival: Effect of Adjustment for Confounding Factors

The results of multivariate Cox proportional hazards analysis are summarized in Table 4. In the unadjusted model, lower PAC was significantly associated with high mortality, but PRA was not. The hazard ratio (95% confidence interval) for lower PAC was 4.752 (2.068–10.921), which was statistically significant (p<0.001). This was true even after exclusion of diabetic subjects. Even after adjusting for age, sex, BMI, duration of HD, inclusion of DM in the all-subject analysis, DBP, %BW reduction, and CTR (model 1), both lower PAC and a lower logarithm of PAC significantly increased the risk of death. The hazard ratios for age, DM, and serum albumin were 1.043 (1.010–1.077, p=0.011), 1.808 (0.672–4.878, n.s.), and 0.457 (0.146–1.437, n.s.), respectively. We further analyzed the prognostic value of PAC, adjusting for the factors in model 1 plus serum albumin (model 2) and model 2 plus serum potassium. The significance of lower PAC became marginal by the addition of albumin in non-DM subjects. Adding potassium to model 2 diminished the significance of a lower logarithm of PAC. The incidence of β-blocker users in the lower PAC group was greater than that in the higher PAC group (20% *vs*. 12.5%), although the difference was not statistically significant. Even after adding β-

Table 4. Results of Cox Proportional Hazards Regression Analysis on Risk of Death

Unadjusted	All subjects ($n=128$)		Nondiabetic subjects ($n=99$)	
	Hazard ratio (CI)	p value	Hazard ratio (CI)	p value
Age	1.061 (1.033–1.090)	<0.001	1.044 (1.011–1.078)	0.009
Male *vs*. female	0.693 (0.352–1.364)	n.s.	1.092 (0.427–2.793)	n.s.
DBP	0.966 (0.935–0.999)	0.043	0.956 (0.923–1.009)	n.s.
Diabetes	2.222 (1.099–4.505)	0.026		
Albumin	0.178 (0.079–0.403)	<0.001	0.110 (0.027–0.456)	0.002
Potassium	0.622 (0.392–0.989)	0.045	0.528 (0.289–0.963)	0.037
Lower PRA (*vs*. high)	1.916 (0.930–3.948)	n.s.	1.916 (0.906–5.566)	n.s.
Lower PAC (*vs*. high)	4.752 (2.068–10.921)	<0.001	4.061 (1.498–11.014)	0.006

Adjusted	Hazard ratio (CI)		
	Model 1	Model 2	Model 3
All subjects			
Lower PAC (*vs*. high)	2.905 (1.187–7.112)*	2.814 (1.133–6.989)*	2.601 (1.045–6.472)*
log PAC (high to low)	2.320 (1.048–5.123)*	2.053 (0.905–4.673)	1.786 (0.787–4.065)
Nondiabetic subjects			
Lower PAC (*vs*. high)	3.204 (1.068–9.611)*	2.846 (0.931–8.703)	2.813 (0.926–8.542)
log PAC (high to low)	3.663 (1.340–10.000)*	3.106 (1.138–8.475)*	2.695 (0.956–7.634)

log, logarithm. Other abbreviations are explained in the first footnote in Table 1. *$p<0.05$. Model 1: adjusted with the following factors: age, sex, BMI, duration of HD, %BW reduction, diabetes (included only for "all subjects"), DBP, CTR. Model 2: model 1 plus albumin. Model 3: model 2 plus potassium.

blocker into model 1, lower PAC was significantly associated with death: the hazard ratio was 2.922 (1.189–7.178, $p=0.0189$).

Survival Rate in Relation to Baseline PRA/PAC or Potassium/PAC in Non-DM Subjects

To exclude the possible contribution of DM to poor prognosis in lower PAC, we evaluated non-DM patients by dividing them into a lower or higher PAC group according to the median baseline value of PAC among these patients. We found that lower PAC was associated with a poorer survival rate than higher PAC even in non-DM subjects (69.4% *vs*. 92%, $p=0.0027$). We further investigated the contribution of RAAS and potassium to survival in non-DM subjects. Based on the median baseline values of PRA and PAC in non-DM subjects, we assigned each of these subjects to one of four groups: a higher PRA/higher PAC (HH), higher PRA/lower PAC (HL), lower PRA/higher PAC (LH), and lower PRA/lower PAC (LL) group. The survival curves based on the baseline PRA/PAC groups are shown in Fig. 3. One-fourth of the lower PAC group did not show lower PRA, hence PAC in this group appeared to be independent of RAAS. The survival rate in this group was as poor as that in the LL subgroup, in which PAC appeared to be dependent on RAAS. Thus the survival rate appeared to depend on PAC but not on RAAS.

Based on the median baseline value of potassium in non-DM subjects, we also assigned each of these subjects to one of four groups: a higher potassium/higher PAC (HkH), higher potassium/lower PAC (HkL), lower potassium/higher PAC (LkH), and lower potassium/lower PAC (LkL) group. Among the lower PAC non-DM subjects, the HkL subgroup was characterized by higher %BW reduction per HD session compared with the LkL subgroup. Although the HkL subgroup showed a significantly higher survival rate than the LkL subgroup, as shown in Fig. 3 (75% *vs*. 64%), 3 of 6 total deaths (50%) in the HkL subgroup were CVD. In contrast, only 1 of 9 total deaths (11%) were CVD, and most other deaths were associated with infection (6 of 8 non-CVD) in the LkL subgroup.

Follow-Up Determination of PAC

We followed up on the annual determination of PAC for 4 years. The mean values of PAC (mean±SEM) from 1996 to 2000 in each group were as follows: 9.7±0.7 ng/dl ($N=64$), 12.4±1.9 ng/dl ($N=52$), 10.6±1.5 ng/dl ($N=45$), 9.7±1.3 ng/dl ($N=41$), and 12.5±3.1 ng/dl ($N=34$) in the lower PAC group; and 100.2±16.6 ng/dl ($N=64$), 74.7±17.8 ng/dl ($N=48$), 90.4±23.2 ng/dl ($N=47$), 79.2±21.6 ng/dl ($N=40$) and 102.2±27.1 ng/dl ($N=38$) in the higher PAC group. Although single PAC measurements in HD patients might vary depending on patient conditions, these data showed that one measurement reflects the values thereafter.

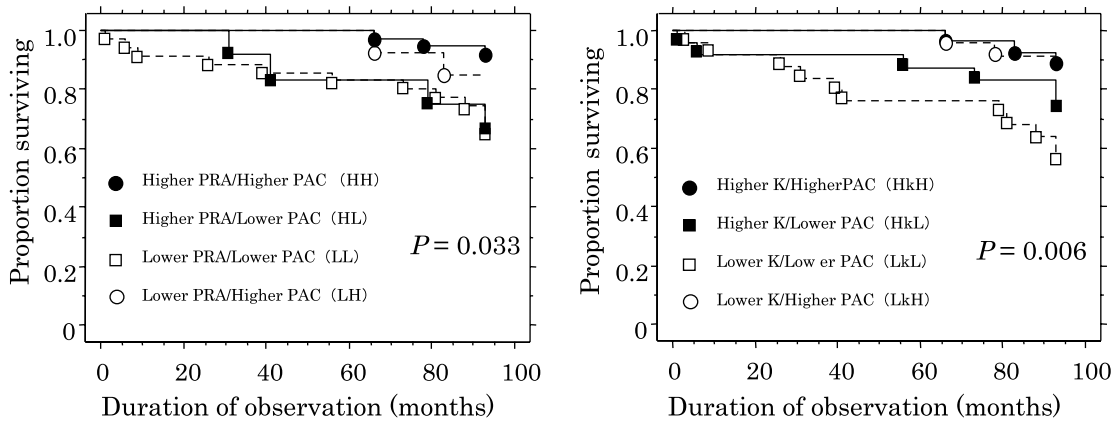

Fig. 3. *Survival curves based on the following baseline categories: plasma renin activity/plasma aldosterone concentration (left panel) or baseline potassium/plasma aldosterone concentration (right panel) in nondiabetic patients. PRA, plasma renin activity; PAC, plasma aldosterone concentration; K, potassium. PAC and potassium were categorized as follows according to their median values in nondiabetic patients: Higher PAC, ≥29.6 ng/dl; lower PAC, <29.6 ng/dl; higher PRA, ≥2.0 ng/ml/h; lower PRA, <2.0 ng/ml/h; higher potassium, ≥5.3 mEq/l; lower potassium, <5.3 mEq/l.*

Discussion

This study shows that a high PAC was commonly found in hypertensive patients undergoing chronic HD, but not associated with all-cause or cardiovascular mortality. A lower rather than a higher PAC was an independent predictor of death in hypertensive patients undergoing chronic HD. This was true even after the exclusion of diabetic subjects.

Many harmful effects of aldosterone on the cardiovascular system have been identified under conditions of salt loading in animal studies (*10, 11*). Endemann *et al*. (*14*) recently reported that such effects of aldosterone are minimal under the condition of low sodium intake. Sato and Saruta suggested that aldosterone-induced organ damage might occur if the aldosterone level and salt status are imbalanced (*15*). In another study, it was reported that the value of PAC was elevated among subjects with chronic renal failure (*16*), who are known to be at high risk for cardiovascular disease (*17*). However, the present study showed that higher PAC was not associated with increased mortality in patients on chronic HD, most of whom show chronic volume and sodium retention. Accumulating evidence suggests that the adverse effect of aldosterone on the heart is accompanied by abnormal activation of RAAS (*3*, *6*, *18*). In the present study, subgroup analysis demonstrated that the three-fourths of higher PAC patients who had higher PRA showed low mortality. Thus, it is possible that the activation of RAAS plays a physiologic but not a pathogenic role in chronic HD patients. Although the precise mechanism of this discrepancy is not clear, it might be that the tubular action of aldosterone, which causes exacerbation of hypertension, did not induce a high rate of sodium retention in the anuric subjects undergoing chronic HD. An alternative explanation involves differences in potassium status. Previous reports have suggested that hypokalemia, which accompanies a high aldosterone concentration, contributes to the adverse effect of aldosterone on the cardiovascular system (*19*, *20*). In the present study, the higher PAC group showed hyperkalemia rather than hypokalemia (Table 1). The higher PAC in HD patients may reflect a physiologic reaction to potassium excess by excretion of potassium into the colon, as previously reported (*21*). Such a physiologic increase in the level of aldosterone may not be harmful. For example, Yanomamo Indians rarely show hypertension despite extremely high PAC levels due to their minimal sodium intake (*22*).

We found that a PAC value higher than the median baseline value was associated with a better rather than a poorer outcome in HD patients. Although we cannot eliminate the possibility that aldosterone itself has a beneficial effect on survival, this observation may indicate that a PAC value lower than the median baseline value is associated with high mortality. This association might have been affected by the difference in the proportion of diabetic patients between the groups. However, a significant association was similarly found even in the 99 nondiabetic subjects. In that nondiabetic group, the significance of lower PAC on survival was marginal when an adjustment was made for serum albumin (model 2 in Table 4). In addition, the significance of both lower PAC and a lower logarithm of PAC on survival became marginal by adding potassium to model 2. Therefore, various conditions associated with lower levels of albumin and hypokalemia may have had an affect on poor survival in the lower PAC group.

Serum albumin was significantly lower in the lower PAC group than in the higher PAC group. A lower level of albumin may reflect malnutrition and/or dilution as a result of volume expansion. However, it is not clear that the lower level of

albumin was due to malnutrition, since covariates indicating nutritional status, such as BMI and total cholesterol, were similar between the groups. Rather, the lower level of albumin in the lower PAC group may have been a reflection of volume expansion. This is because the CTR in the lower PAC group was relatively greater, although the interdialytic BW gain in this group was significantly smaller, than in higher PAC group (Table 1), indicating that the mean volume status in the lower PAC group during a week was higher than that in the higher PAC group.

In the subgroup analysis, the cause of death was quite different between the LkL and HkL subgroups. Most of the deaths in the LkL subgroup, which was characterized by lower levels of serum potassium, were due to infection. The lower levels of serum potassium in the LkL subgroup may have been due to a decrease in food intake, since the interdialytic BW gain in the LkL subgroup was significantly smaller than that in the HkL subgroup (data not shown). It is unknown whether the association of lower potassium and death due to infection was causative or the result of residual confounding factors in those with worse general condition. However, potassium may have had a pathogenic role. A lower level of potassium may cause abnormal immunity, since activation of the voltage-dependent potassium channel, which is inactivated by hypokalemia, has been shown to have pivotal role in the immune response of T lymphocytes (*23*).

There were several limitations in this study. We cannot fully rule out the role of aldosterone excess in the pathogenesis of cardiovascular disease, since information is lacking about the morbidity of cardiovascular events. In addition, circulating aldosterone may not accurately reflect the production of aldosterone. Some studies have shown that aldosterone produced extraadrenally (*24*, *25*) may be involved in the pathogenesis of cardiovascular damage (*26*). Therefore, we cannot exclude the possibility that locally produced aldosterone causes cardiovascular disease and thereby affects outcome. Finally, the value of PAC at pre HD could be changed either after HD or under a condition with salt loading (*9, 13*). It has been reported that inadequate suppression of PAC after salt loading rather than the absolute value of PAC was associated with left ventricular hypertrophy in hypertensive subjects (*9*). Kigoshi *et al*. reported that the impaired response of aldosterone to adrenocorticotropic hormone, but not the absolute value of aldosterone, predicted the progression to end-stage renal failure among diabetic patients (*27*). Since we did not examine the value of PAC under these conditions, we could not determine the pathogenic role of aldosterone in chronic HD patients.

In conclusion, we found that a PAC value higher than the median baseline value was not associated with the increase in total and cardiovascular deaths, even under the condition of chronic volume excess, and that lower rather than higher PAC relative to the median baseline value was a significant predictor of death in hypertensive patients undergoing chronic HD. The poor survival in patients with an aldosterone level lower than the median baseline value may be related to volume retention and lower potassium. Patients undergoing chronic HD often show chronic volume excess and/or potassium retention. Therefore, the role of aldosterone in such patients may be different from that in non-HD patients. Further prospective studies will be needed to elucidate the physiologic and pathogenic roles of aldosterone in HD patients.

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