

Low diastolic blood pressure, hypoalbuminemia, and risk of death in a cohort of chronic hemodialysis patients

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Low diastolic blood pressure, hypoalbuminemia, and risk of death in a cohort of chronic hemodialysis patients. In a previous report, we showed that nutritional status and especially serum albumin had great predictive value for death in chronic hemodialysis patients, whereas blood pressure did not. In the present study, we analyzed the causes of death in consideration of the relationship between serum albumin and blood pressure. A total of 1,243 Okinawan patients (719 males, 524 females) undergoing hemodialysis in January 1991 were followed up through the end of 1995. Three hundred forty-two of the patients died, 45 received transplants, and 12 were transferred by the end of the follow-up period. The total duration of observation was 5,110.3 patient-years. Blood pressure as well as clinical and laboratory variables were determined immediately prior to the first dialysis session in January 1991. The crude death rate was 40.0% when the diastolic blood pressure (DBP) <70 mm Hg, 35.0% at 70 to 79 mm Hg, 25.0% at 80 to 89 mm Hg, 25.0% at 90 to 99 mm Hg, and 13.0% at >100 mm Hg. The death rate showed an inverse correlation with DBP. DBP showed a significant positive correlation with serum albumin ($r = 0.137, P < 0.001$) and age ($r = -0.325, P < 0.0001$). The adjusted odds ratio (95% confidence interval) of death was 0.84 (0.71 to 0.99) with 10 mm Hg increments in DBP when the reference DBP was less than 69 mm Hg. Low DBP may be a manifestation of malnutrition and/or cardiovascular disease in chronic hemodialysis patients. Target DBP levels may be higher levels in chronic hemodialysis patients than the general population.

The prognosis of chronic dialysis patients is poor compared to that of the general population [1]. Therefore, every effort must be made to detect potentially treatable causes of death in such patients. Charra et al. reported that the best survival was associated with control of both nutritional factors and blood pressure [2, 3]. Nutritional factors have been shown to be a strong predictor of mortality in chronic dialysis patients [4, 5]. However, Churchill et al [6] found that the effects of blood pressure on survival were not significant as did the present authors [4]. Recently, an increasing number of elderly and sick patients have been accepted for dialysis [1, 7]. The level to which blood pressure should be lowered is still under debate, even in the general population [8]. In dialysis patients, who are highly selected and have multiple

comorbid conditions, data that assess the relative contribution of each risk factor are lacking [9, 10].

The aim of the present study was to determine the relationship between the baseline levels of serum albumin and blood pressure, and to analyze the causes of death in chronic dialysis patients. We focused on the effects of these variables on the survival of the patients. Target blood pressure levels were determined with respect to the mortality rate. The results confirm the significance of hypoalbuminemia and low diastolic blood pressure on survival.

Methods

A total of 1,243 patients (719 males, 524 females) undergoing hemodialysis in January 1991 in Okinawa, Japan were examined and prospectively followed up until the end of 1995. The demographics of this patient population were reported previously [1,4]. Briefly, patients with end-stage renal disease who survived at least one month on dialysis were registered in the Okinawa Dialysis Study (OKIDS) registry. Between 1971 and 1990, a total of 1,982 patients were registered (824 females and 1,158 males). Patients who died ($N = 605$), underwent renal transplant ($N = 75$), were transferred ($N = 23$), or were placed on CAPD ($N = 36$) were excluded. All outcomes were known and confirmed. Frequency of dialysis was 0.9% once-weekly, 15.4% twice-weekly, and 83.7% thrice-weekly [4]. Baseline data of laboratory and clinical variables were obtained before the first dialysis session in January 1991. Similarly, the baseline blood pressure was recorded in order to establish a pre-dialysis blood pressure in January 1991. Mean arterial blood pressure (MAP) was calculated as diastolic blood pressure (DBP) + 1/3[systolic blood pressure (SBP) - DBP].

Administration of antihypertensive drugs was confirmed by reviewing patient charts. Antihypertensive drugs were categorized as follows: calcium channel blockers, ACE inhibitors, beta-blockers, centrally acting drugs, alpha-blockers, and vasodilators. Diuretics were not included. Six hundred and forty-six patients (52.0%) were prescribed at least one antihypertensive drug. In the patients receiving antihypertensives ($N = 646$), calcium channel blockers were used in 552 patients (80.8%), ACE inhibitors in 216 patients (33.4%), beta blockers in 159 patients (24.6%), centrally acting agents in 77 patients (11.9%), alpha blockers in 45 patients (7.0%), and vasodilators in 22 patients (3.4%).

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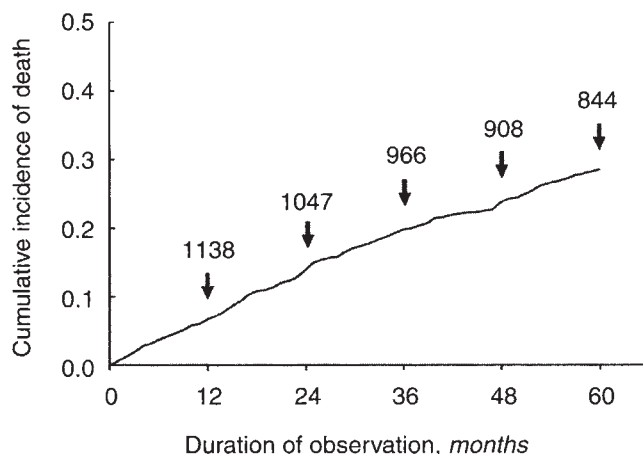


Fig. 1. Cumulative incidence of death in cohort of 1,243 chronic hemodialysis patients. The follow-up period was 1991 through 1995. Figures are number of patients at risk.

Causes of death were categorized as: infection, withdrawal, cardiac, sudden death, vascular, and others [1, 11]. Briefly, the final decision was made by one of the author (K.I.) by reviewing the medical charts and after discussion with the physician. Vascular death was restricted only those who had X-ray, CT brain scan, and laboratory data. In case of long-term hospitalization, direct cause of death was taken for the cause of death. All patients were followed up until death, renal transplantation, transfer outside of Okinawa, or the end of 1995. The number of deaths, transplants, and transfers were 342, 45, and 12, respectively. The total duration of observation was 5,110.3 patient-years.

Statistical analysis was performed with the SAS package using the database of the Okinawa Dialysis Study (OKIDS) [1, 4]. Student's *t*-tests and chi square tests were used. Pearson correlation coefficients were calculated in order to investigate the relationships between the pertinent clinical variables. Multiple logistic analysis was performed in order to determine the significance of each variable with respect to survival. Survival curves were drawn by the Kaplan-Meier method. *P* values less than 0.05 were considered statistically significant. Data were expressed as mean \pm SEM.

Results

Figure 1 shows the cumulative incidence of death. Death increased linearly over time, and reached 28.3% of five years. The total number of deaths was 342 (200 men and 142 women); 78 (22.8%) cardiac, 62 (18.1%) infection, 56 (16.4%) withdrawal, 26 (7.6%) sudden death, 67 (19.6%) vascular, and 53 (15.5%) other causes. In these categories, cardiac, withdrawal, sudden death, and vascular death are basically cardiovascular origin.

Table 1 shows the baseline variables of patients who died and who survived. In the deceased group, age was greater and duration of hemodialysis was shorter, whereas the dose of dialysis was lower than that in the survival group. Body height and weight were significantly lower in the deceased group. No significant difference between the groups was observed in systolic blood pressure, but diastolic blood pressure was significantly lower in the deceased group. Total protein, serum albumin, total cholesterol, triglyceride, BUN, and serum creatinine were also signifi-

Table 1. Comparison of the baseline variables between patients who died and who survived which were obtained at the entry to the study (January 1991)

| Clinical | Total N = 1,186 | Died N = 342 | Survived N = 844 | P Value ^a |
|--------------------------------------|--------------------|-----------------|---------------------|----------------------|
| Age years | 52.4 (0.4) | 62.9 (0.7) | 48.8 (0.5) | 0.0001 |
| Duration of HD months | 62.4 (1.5) | 54.4 (2.6) | 65.6 (1.8) | 0.0004 |
| Dose of dialysis m ² hr/W | 18.2 (0.2) | 16.4 (0.3) | 19.0 (0.2) | 0.0001 |
| Body height meters | 1.56 (0.01) | 1.54 (0.01) | 1.57 (0.01) | 0.0001 |
| Body weight kg | 53.0 (0.3) | 50.6 (0.5) | 54.0 (0.4) | 0.0001 |
| Body mass index kg/m ² | 21.6 (0.1) | 21.4 (0.2) | 21.7 (0.1) | NS |
| Systolic BP mm Hg | 151.5 (0.7) | 152.3 (1.3) | 151.2 (0.8) | NS |
| Diastolic BP mm Hg | 80.8 (0.4) | 77.1 (0.7) | 82.3 (0.5) | 0.0001 |
| Total protein g/dl | 6.5 (0.02) | 6.4 (0.03) | 6.6 (0.02) | 0.0001 |
| Serum albumin g/dl | 3.9 (0.01) | 3.7 (0.03) | 4.0 (0.02) | 0.0001 |
| Total cholesterol mg/dl | 171.1 (1.2) | 164.2 (2.2) | 173.8 (1.4) | 0.0002 |
| Triglyceride mg/dl | 161.9 (3.1) | 141.6 (5.0) | 170.2 (4.3) | 0.0001 |
| BUN mg/dl | 85.8 (0.6) | 82.2 (1.1) | 87.2 (0.7) | 0.0001 |
| Serum creatinine mg/dl | 13.1 (0.1) | 11.4 (0.2) | 13.8 (0.1) | 0.0001 |
| Serum uric acid mg/dl | 8.2 (0.1) | 8.1 (0.1) | 8.3 (0.1) | NS |
| Smoker % | 23.4 | 20.5 | 24.6 | NS |
| Drinker % | 20.3 | 12.3 | 23.6 | 0.0001 |
| Diabetes mellitus % | 17.6 | 35.4 | 10.4 | 0.0001 |
| Antihypertensives % | 51.7 | 53.2 | 51.1 | NS |
| Male % | 58.1 | 55.3 | 59.2 | NS |

Patients who received renal transplantation (*N* = 45) or were transferred outside Okinawa (*N* = 12) during the study period were excluded. Numbers in parentheses denote SEM. Abbreviations are: HD, hemodialysis; BP, blood pressure; BUN, blood urea nitrogen; NS, not significant. Duration of HD refers to how long the patients had been on dialysis prior to entry into the study.

^a *P* Value is died vs. survived.

cantly lower in the deceased group. Survivors and died patients had a similar percent of use of antihypertensives. Comparison of clinical variables between those who were receiving once or twice dialysis per week and those on thrice per week were summarized in Table 2. Women were more common in those who were dialyzed less than three times per week. There was no difference in serum albumin and death rate between the groups.

Table 3 shows the mean (SEM) levels of systolic and diastolic blood pressure in each baseline serum albumin category. A significant correlation between baseline serum albumin and diastolic blood pressure was observed ($r = 0.137$, $P = 0.0001$). The proportion of renal transplantation and transferral outside of Okinawa were higher in patients with normal serum albumin.

Table 4 shows the death rate and mean (SEM) age of the patients in each systolic, diastolic, and mean arterial pressure category. The death rate and diastolic blood pressure were inversely correlated. Since the number of patients with SBP less than 119 mm Hg was small, all such patients were considered together.

Table 5 shows the number (%) of deaths at each level of baseline serum albumin. In patients with hypoalbuminemia (less than 3.5 g/dl) the most common causes of death were withdrawal and cardiac. In normo-albuminemia patients (greater than 4.0 g/dl), vascular and infection were the leading causes of death.

Figure 2 shows the survival curves in relation to the baseline levels of serum albumin. In patients with hypoalbuminemia, the five-year proportion of survival was less than 50%. The survival curves for each baseline level of systolic and diastolic blood pressure are shown in Figures 3 and 4. No appreciable differences were observed among the subgroups of SBP. Higher baseline DBP levels were associated with a high proportion of survival.

Table 2. Comparison of the baseline variables between patients who were receiving once or twice dialysis per week and those of thrice dialysis per week at the entry to the study (January 1991)

| Clinical | Frequency of dialysis per week | | P value |
|--------------------------------------|--------------------------------|-------------------|---------|
| | Once & twice N = 192 | Thrice N = 994 | |
| Age years | 56.1 (1.2) | 51.6 (0.4) | 0.0006 |
| Duration of HD months | 29.0 (2.7) | 68.8 (1.6) | 0.0001 |
| Dose of dialysis m ² hr/W | 10.3 (0.2) | 19.8 (0.2) | 0.0001 |
| Body height meters | 1.54 (0.006) | 1.57 (0.003) | 0.0001 |
| Body weight kg | 49.1 (0.7) | 53.8 (0.3) | 0.0001 |
| Body mass index kg/m ² | 20.7 (0.2) | 21.8 (0.1) | 0.0001 |
| Systolic BP mm Hg | 153.9 (1.6) | 151.1 (0.8) | NS |
| Diastolic BP mm Hg | 78.8 (1.0) | 81.2 (0.4) | 0.027 |
| Total protein g/dl | 6.6 (0.04) | 6.5 (0.02) | NS |
| Serum albumin g/dl | 3.9 (0.04) | 3.9 (0.02) | NS |
| Total cholesterol mg/dl | 171.5 (3.2) | 171.0 (1.3) | NS |
| Triglyceride mg/dl | 136.6 (5.9) | 166.9 (3.9) | 0.0001 |
| BUN mg/dl | 89.4 (1.6) | 85.1 (0.6) | 0.012 |
| Serum creatinine mg/dl | 11.8 (0.3) | 13.4 (0.1) | 0.0001 |
| Serum uric acid mg/dl | 8.3 (0.1) | 8.2 (0.1) | NS |
| Smoker % | 18.2 | 24.5 | NS |
| Drinker % | 13.5 | 21.6 | 0.011 |
| Diabetes mellitus % | 23.4 | 16.5 | 0.021 |
| Antihypertensives % | 52.6 | 51.5 | NS |
| Male % | 47.9 | 60.1 | 0.002 |
| Death rate % | 32.8 | 28.1 | NS |

Patients who received renal transplantation (N = 45) or were transferred outside Okinawa (N = 12) during the study period were excluded. Numbers in parentheses denote SEM. Abbreviations are: HD, hemodialysis; BP, blood pressure; BUN, blood urea nitrogen; NS, not significant. Duration of HD refers to how long the patients had been on dialysis prior to entry into the study.

Table 3. Relationship between serum albumin level and blood pressure

| | Baseline serum albumin g/dl | | | |
|-----------------------------|-----------------------------|--------------------|--------------------|-----------------|
| | <3.5 N = 206 | 3.5–3.9 N = 501 | 4.0–4.4 N = 373 | 4.5≤ N = 139 |
| SBP mm Hg | | | | |
| mean | 152.4 | 151.2 | 151.7 | 151.0 |
| SEM | 1.8 | 1.1 | 1.2 | 1.8 |
| DBP mm Hg | | | | |
| mean | 78.3 | 80.2 | 82.1 | 84.1 |
| SEM | 0.9 | 0.6 | 0.6 | 1.2 |
| Renal transplantation | 2 (1.0%) | 12 (2.4%) | 20 (5.4%) | 11 (7.9%) |
| Transferred outside Okinawa | 3 (1.5%) | 3 (0.6%) | 2 (0.5%) | 4 (2.9%) |

Abbreviations are: SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 6 shows the causes of death in relation to age at start of the study. The leading cause of death was different in each age group. In the 0 to 44 and 45 to 54 year-old groups, vascular disease was the most common causes of death. In the 55 to 64 year-old group, cardiac disease was the most common cause. Whereas in the older than 65-year-old group, the most common cause was withdrawal from dialysis.

Table 7 summarizes the results of multiple logistic analysis. The adjusted odds ratio (95% confidence interval) for death was 0.84 (0.71 to 0.99) for diastolic blood pressure and 0.77 (0.64 to 0.91) for serum albumin. The variables included were sex, age, duration of dialysis, diabetes mellitus, smoking, dose of dialysis, body mass

Table 4. Number of total and deceased patients in each stratum of systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP)

| | Patients | | Death rate | Age of patients mean (SEM) |
|-----------|----------|------|------------|----------------------------|
| | Exposed | Died | | |
| SBP mm Hg | | | | |
| –79 | 3 | 2 | 0.67 | 66.9 (6.9) |
| 80–99 | 10 | 2 | 0.20 | 54.7 (2.7) |
| 100–119 | 58 | 15 | 0.26 | 54.0 (2.0) |
| 120–139 | 227 | 56 | 0.25 | 52.9 (0.9) |
| 140–159 | 404 | 102 | 0.25 | 51.8 (0.7) |
| 160–179 | 353 | 111 | 0.31 | 52.1 (0.8) |
| 180– | 188 | 54 | 0.29 | 52.1 (1.0) |
| DBP mm Hg | | | | |
| –69 | 154 | 61 | 0.40 | 58.7 (1.2) |
| 70–79 | 267 | 93 | 0.35 | 56.8 (0.9) |
| 80–89 | 426 | 108 | 0.25 | 51.9 (0.6) |
| 90–99 | 232 | 58 | 0.25 | 50.1 (0.9) |
| 100– | 164 | 22 | 0.13 | 43.0 (1.0) |
| MAP mm Hg | | | | |
| –89 | 178 | 59 | 0.33 | 56.0 (1.2) |
| 90–99 | 235 | 68 | 0.29 | 55.1 (0.9) |
| 100–109 | 374 | 111 | 0.30 | 52.6 (0.7) |
| 110–119 | 245 | 63 | 0.26 | 51.5 (0.9) |
| 120– | 211 | 41 | 0.19 | 46.5 (0.9) |

Age of patient was calculated at start of study (Jan. 1, 1991). Abbreviation SEM is standard error of mean. Follow-up period was 1991 through 1995.

Table 5. Causes of death and baseline serum albumin

| Cause of death | Baseline serum albumin g/dl | | | | Total |
|------------------|-----------------------------|-----------|-----------|----------|-----------|
| | <3.5 | 3.5–3.9 | 4.0–4.4 | 4.5≤ | |
| Infection | 19 (18.6) | 26 (17.2) | 12 (18.5) | 5 (22.7) | 62 (18.2) |
| Withdrawal | 30 (29.4) | 16 (10.6) | 9 (13.8) | 1 (4.5) | 56 (16.5) |
| Cardiac | 20 (19.6) | 43 (28.5) | 9 (13.8) | 6 (27.3) | 78 (22.9) |
| Sudden death | 7 (6.9) | 10 (6.6) | 4 (6.2) | 4 (18.2) | 25 (7.4) |
| Vascular | 15 (14.7) | 27 (17.9) | 22 (33.8) | 3 (13.6) | 67 (19.7) |
| Others | 11 (10.8) | 29 (18.2) | 9 (13.8) | 3 (13.6) | 52 (15.3) |
| Number of deaths | 102 (100) | 151 (100) | 65 (100) | 22 (100) | 340 (100) |
| exposed | 206 | 501 | 373 | 139 | 1,219 |
| Death rate | (49.5) | (30.1) | (17.4) | (15.8) | (27.9) |

Follow-up period was 1991 through 1995. Total number of deaths was 342. Two patients had no baseline serum albumin data. Parentheses denote percentage.

index, serum creatinine, systolic and diastolic blood pressure, serum albumin. The crude death rate was highest as 57.3% in a subgroup of patients (N = 89) with low serum albumin (<3.5 g/dl) and low diastolic blood pressure (<80 mm Hg), and lowest as 11.1% in a subgroup of patients (N = 63) with high serum albumin (≥4.5 g/dl) and high diastolic blood pressure (≥90 mm Hg).

Discussion

Hypertension is usually present at the initiation of dialysis therapy. With the start of regular hemodialysis, most patients become normotensive by attaining dry weight. However, few studies have investigated the significance of control of blood pressure in maintenance dialysis patients [12]. Charra et al [2, 3] demonstrated very good control of blood pressure and excellent

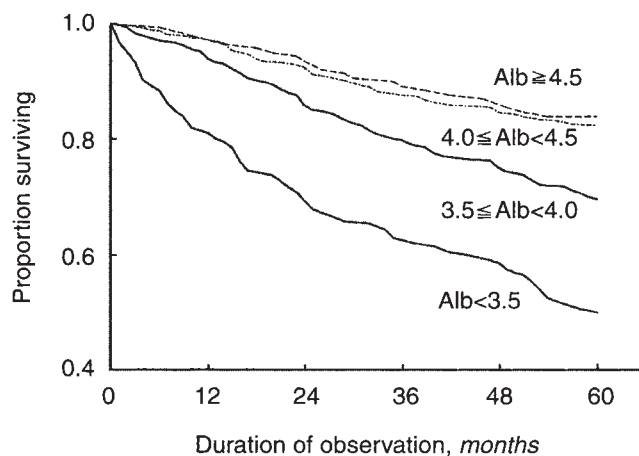


Fig. 2. Survival curves, calculated by method of Kaplan-Meier, for each baseline level of serum albumin. Follow-up period was 1991 through 1995.

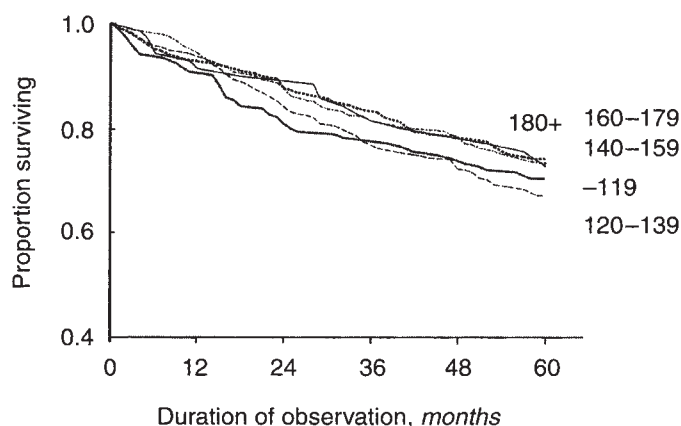


Fig. 3. Survival curves, calculated by method of Kaplan-Meier, for each baseline level of systolic blood pressure. Follow-up period was 1991 through 1995.

prognosis by prescribing a long slow dialysis. We [1, 4] and others [5-7, 13] have been prescribing a dose of dialysis lower than that of Charra et al. Recently, the number of older and sicker patients accepted for dialysis has been increasing [1, 7]. In these patients, rapid ultrafiltration may cause a premature drop in blood pressure before they reach dry weight. The use of shortened dialysis and noncompliance in adult dialysis patients [14] may further increase the incidence of hypertension and deteriorate nutritional status.

The essential hypertension population consists of those of salt-sensitive and non-salt-sensitive subjects. Manipulation of salt intake within the range of 2 to 30 g/day results in little or no observable change for the general population as a whole [15]. Therefore, assuming that all dialysis patients are salt sensitive is not realistic [6, 12]. In the well known paper of Vertes et al [13], blood pressure was followed for less than six months, a relatively short period. Reported blood pressure levels were approximately 150 mm Hg in SBP and 80 to 90 mm Hg in DBP, which agrees with our data (Tables 3 and 4). Moreover, the relationship between volume and vasoconstrictor factors is complex [16-18]. Potent antihypertensive drugs have been developed recently;

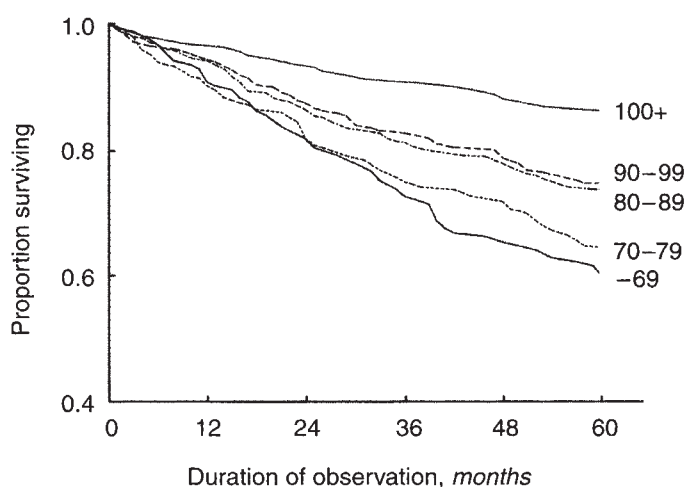


Fig. 4. Survival curves, calculated by method of Kaplan-Meier, for each baseline level of diastolic blood pressure. Follow-up period was 1991 through 1995.

Table 6. Causes of death and age at start of study

| Cause of death | Age at start of study years | | | | Total |
|------------------|-----------------------------|-----------|-----------|-----------|-----------|
| | 0-44 | 45-54 | 55-64 | 65+ | |
| Infection | 5 (13.2) | 8 (16.7) | 15 (15.6) | 34 (21.2) | 62 (18.1) |
| Withdrawal | 2 (5.3) | 5 (10.4) | 8 (8.3) | 41 (25.6) | 56 (16.4) |
| Cardiac | 10 (26.3) | 5 (10.4) | 29 (30.2) | 34 (21.3) | 78 (22.8) |
| Sudden death | 5 (13.2) | 5 (10.4) | 6 (6.3) | 10 (6.3) | 26 (7.6) |
| Vascular | 15 (39.4) | 19 (39.6) | 18 (18.8) | 15 (9.4) | 67 (19.6) |
| Others | 1 (2.6) | 6 (12.5) | 20 (20.8) | 26 (16.2) | 53 (15.5) |
| Number of deaths | 38 (100) | 48 (100) | 96 (100) | 160 (100) | 342 (100) |
| exposed | 433 | 268 | 284 | 258 | 1,243 |
| Death rate | 8.8% | 17.9% | 33.8% | 62.0% | 27.5% |

Follow-up period was 1991 through 1995. Age was calculated on January 1, 1991. Parentheses denote percentage.

therefore, our patient population included no cases of bilateral nephrectomy for the control of blood pressure.

Our results suggest that the optimal level of blood pressure associated in terms of death rate is higher in dialysis patients than in the general population [8, 19-21]. Erroa et al [22] reported that low DBP was associated with visceral and somatic malnutrition as well as a high mortality rate in dialysis patients. Relative hypotension was a potent marker of mortality in dialysis patients [10]. Hypotension may reflect both the severity of disease, ischemic heart disease and/or cardiomyopathy, and the intensity of therapy used to treat the disease. A close correlation was observed between DBP and serum albumin or patient's age (Tables 3 and 4). Serum albumin is a strongest predictors of death in dialysis patients [4, 5, 23, 24], and even in patients at baseline who are starting dialysis therapy [25]. Therefore, multiple logistic analysis is required in order to investigate the role of blood pressure adjusted with other confounding predictors of death. In a short-term follow-up study, the effect of blood pressure on mortality was not found to be significant [4, 6].

Dialysis patients are highly selected and have multiple risk factors of cardiovascular disease. They are often malnourished [4, 5, 23, 24] and have comorbid conditions in addition to renal

Table 7. Multiple logistic analysis of clinical predictors of death in cohort of chronic hemodialysis

| | Odds ratio | |
|---|-------------------------|-----------------------|
| | 95% confidence interval | |
| | Not adjusted | Adjusted ^a |
| Systolic blood pressure (vs. less than 119 mm Hg) 20 mm Hg increments | 1.09 (0.97–1.22) | 1.12 (0.95–1.33) |
| Diastolic blood pressure (vs. less than 69 mm Hg) 10 mm Hg increments | 0.73 (0.65–0.82) | 0.84 (0.71–0.99) |
| Serum albumin (vs. <3.5 g/dl) | 0.53 (0.45–0.61) | 0.77 (0.64–0.91) |

Follow-up period was 1991 through 1995.

^a Adjusted for other potential predictors of death such as sex, age, duration of dialysis, diabetes mellitus, smoking, dose of dialysis, body mass index, serum creatinine, and variables in table.

failure [7, 26–28] at the initiation of dialysis. In our cohort of dialysis patients, systolic blood pressure was not observed to increase with age [29]. A similar phenomenon was reported in the inhabitants of undeveloped countries, agreeing with the established clinical effects of salt restriction [30]. However, lack of obesity and weight gain with advance of age and change of lifestyle were other possible explanations [30]. Obviously, the lifestyle of dialysis patients is quite different from that of the general population.

Elevated DBP, but not decreased DBP, was associated with a high mortality rate in the Diaphane study [23]. The background of the present patient population was different in several ways. First, the duration of dialysis is different. The mean duration of hemodialysis in the present study was approximately 60 months at the start of the study, so many high-risk patients may have died before entering the study. Actually, the peak hazard for cardiovascular death was less than four years of dialysis [11]. Second, our study population included a higher proportion of diabetic patients, who are known to have poor survival [1]. Third, a precise relationship between blood pressure and nutritional status was not shown in their study.

Calcium channel blockers were the most frequently used antihypertensive drugs in our registry [29], and have the distinct advantage of short duration of action and rapid onset when administered sublingually [31]. Although the dialysance of these drugs is not well known [32], no serious side effects were noted, except for occasional hypotension. ACE inhibitors may cause anaphylactoid reaction with the use of PAN membrane dialyzers [33], but we have experienced no such cases.

The use of erythropoietin may increase blood pressure [34]. We do not know the incidence of hypertension in relation to the use of antihypertensive drugs before the era of erythropoietin in our registry. Erythropoietin was not funded for general clinical use in Japan until April 1990. No case of death related to the hypertensive effect of erythropoietin occurred during the observation period.

In the present cohort study, the baseline blood pressure was measured immediately prior to the first dialysis session in 1991. Correlation of the one-point blood pressure and the one month average blood pressure was excellent in both systolic and diastolic blood pressures [29]. Furthermore, we evaluated the determinants of blood pressure by stepwise regression and univariate analysis.

For systolic blood pressure, a positive association was found with male, diabetes mellitus, total cholesterol, use of antihypertensives, year at start of dialysis, and negative associations were age, triglyceride, total protein. For diastolic blood pressure, a positive association was found with male, total cholesterol, use of antihypertensives, and dose of dialysis, and negative associations were age and triglyceride.

The use of baseline blood pressure is recommended over the use of time-averaged blood pressure in prospective studies [35]. The dose of antihypertensive drugs immediately preceding dialysis may be reduced or omitted to minimize the risk of hypotension during the procedure [31]. Instructions given to patients about taking antihypertensive medication before hemodialysis varied among physicians in our multi-center study. Using 48-hour blood pressure monitoring, Cheigh et al reported no apparent difference in blood pressure prior to hemodialysis and mean blood pressure in 53 chronic dialysis patients [12]. Hypertension was found to be inadequately controlled.

In order to perform regular hemodialysis, stable hemodynamics and good blood access are mandatory. Patients with low DBP may show unstable hemodynamics during dialysis, and blood access may not be adequate to perform regular dialysis. Moreover, physicians in charge of the dialysis session may choose a higher blood pressure [31] and not increase the ultrafiltration rate, intending to perform “asymptomatic dialysis.” This practice may lead to fluid overload, even in patients with normal cardiac function. The clinical significance of these practices need to be studied further. Blood access thrombosis frequently occurs in patients with low serum albumin [6]. Hypoalbuminemia is potentially reversible risk factor of ischemic heart disease [36].

The present results do not exclude the importance of blood pressure control [37–40], indeed, hypertension is a strong predictor of stroke in this patients population [38]. The deleterious effect of lowering blood pressure in treated hypertensive patients is known as the J curve phenomenon [8]. Preceding illness is thought to lower blood pressure or DBP, precipitating death from coronary heart disease [8] and probably cardiomyopathy [10]. The causes of skewed relationship between the crude death rate and blood pressure in chronic dialysis patients were not determined in this study. We suspect that the high prevalence of cardiovascular disease [26–28] is playing a role, at least partly. The best survival rate in dialysis patients was obtained by control of both nutritional status and blood pressure [2]. Regimens of antihypertensive treatment and dialysis prescription may need to be re-evaluated, especially in patients with hypoalbuminemia and low DBP.

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